Risk factors for the development of impulse control disorders in Mexican subjects with Parkinson's disease.

Factores de riesgo para el desarrollo de trastornos del control de impulsos en sujetos mexicanos con enfermedad de Parkinson.

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ABSTRACT

Objectives: Impulse control disorders (ICDs) are behaviors that are performed repeatedly to the point of interfering with the patient's functionality and daily life, without regard for their consequences and with the sole purpose of obtaining immediate gratification. ICDs have been related to dopaminergic treatment. This study analyzes the association of different risk factors for the development of ICD in the Mexican population.

Methods: a cross-sectional study was carried out. The data collected affects the years 2021 to 2023. Data was collected through structured interviews including age, gender, year of symptom onset, year of diagnosis, levodopa equivalent dose, antiparkinsonian treatment, and history of smoking and alcohol use was evaluated.

Results: A total of 244 patients diagnosed with PD were included, of whom 146 (59.8%) were men and 98 (40.2%). The mean age was 63+/-12.10 years. A total of 35 (14.3%) patients with ICD (ICD-PD) were found; the non-ICD group included 209 subjects(85.7%).

When analyzing antiparkinsonian drugs, a higher use of dopamine agonists was found in the ICD group but did not reach statistical significance (p=0.078).Only the variable alcoholism was identified as a risk factor in the logistic regression , as can be seen in its P value 0.034, the OR value IS 2.55, indicating that patients with alcoholism have a 2.5 times higher risk of developing ICD.

The rest of the variables did not show statistically significant p-values.

Conclusions: History of alcohol use was the main associated risk factor with the development of ICD.

Keywords: Parkinson's disease, Impulse control disorder, risk factors.

BACKGROUND

Parkinson's disease (PD) is a complex, adult-onset neurodegenerative process being the second most common neurodegenerative disease after Alzheimer's disease [1]. Neuronal loss in the substantia nigra, which causes striatal dopamine deficiency, and intracellular inclusions containing aggregates of α-synuclein, are the neuropathological hallmarks of Parkinson's disease [2].

Although there is currently no treatment that halts the progression of PD, current treatment aims to improve symptoms by (a) replacing dopamine by its precursor, (b) inhibiting of the enzymes that break down dopamine [3].

A group of symptoms in PD are non-motoric [4], such as sleep disorders, cognitive disorders and mood disorders. [5,6]

Impulse control disorders (ICDs) and related impulsive and compulsive behaviors (ICBs) have been increasingly recognized in the context of PD and have been mainly related to dopaminergic treatment [7].

According to published literature 10% of the overall population with PD meets the criteria for at least one episode of ICD in their life [8].

ICDs are behaviors that are carried out repeatedly, excessively, and compulsively to the extent that they interfere with the patients functionality and daily life, regardless of their consequences and solely for the purpose of immediate gratification. Their severity can vary, ranging from a mild change in behavior noticed by the patient and their family without functional implications and even improving their quality of life to a major problem that involves economic ruin, legal issues, job loss, divorce, or health risks. Among other risk factors, a personal history of alcoholism or smoking, male gender, and early onset age are found [9].

ICDs are more common in patients with PD than in the general population. They are related to treatment with dopaminergic agonists as they increase the risk by 2 to 3.5 times with an average time between starting the medication and the presence of ICDs being 23 months [10].

ICDs are not typically spontaneously reported by the patient which is why inquiring about these symptoms may be the only

way to detect and manage a serious socio-familial problem. [11].

OBJECTIVE

To determine the frequency of known risk factors for ICD in Mexican patients with PD.

METHODS

A cross-sectional study of patients diagnosed with PD according to the Movement Disorders Society (MDS) criteria [12] was conducted at the National Institute of Neurology and Neurosurgery in the Movement Disorders Clinic. The collected data ranged from 2021 to 2023 and was obtained through a structured interview including variables such as age, gender, year of symptom onset, year of diagnosis, socioeconomic status, equivalent levodopa dose (LED), dopaminergic medications including LD, DA, amantadine and monoamine oxidase type B inhibitors (MAOIs) to directly compare different antiparkinsonian treatment doses [13]. The presence or absence of smoking (defined for our study as regular tobacco consumption) or alcohol use (defined for our study as regular alcohol intake) was evaluated and MDS-Unified

Parkinson's Disease Rating Scale (MDS-UPDRS)item 1.6 on dopaminergic dysregulation was taken as a nominal variable [14] indicating whether it was present or not.

Smoking habits was operationally defined as follows: Categorization of an individual as a current smoker, former smoker, or never smoker, based on self-report or clinical assessment. Secondhand smoke exposure is the extent to which an individual is exposed to smoke from others who smoke.

The operational definition for alcohol intake included: the characterization of an individual's drinking habits such as moderate, heavy, or occasional drinking. Alcohol Dependency or Alcohol Use Disorder was defined as the presence and severity of symptoms associated with alcohol dependency using standardized diagnostic criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).

All subjects were evaluated by a neurologist specialized in movement disorders. Subjects were divided into two groups according to ICD presence: the ICD-PD group and Non-ICD group.

Presence of ICDs was assessed using the Questionnaire for Impulsive-Compulsive Disorders (QUIP-RS). The QUIP-RS is a brief, self-reported or rater-administered rating scale to assess the frequency and severity of ICD symptoms and related behaviors reported to occur in PD [15] and it was evaluated as

a nominal variable by having a point on the scale considering it as a positive result for the presence of this diagnosis. It will be analyzed as a nominal variable to determine the number of patients who reported self-perceived impulsive behavior at the time of application of the scale if they presented behaviors.

LEDD was calculated as published elsewhere [13].

Statistical analysis

A normality test was performed resulting in a non-normal distribution. Consequently, the statistical test, used for the nominal variables, was chi-square, while quantitative variables were analyzed using the Mann-Whitney U test.

To investigate the relationship between the presence or absence of impulse control disorders and known risk factors, potential confounding variables were added to a logistic regression model as independent variables. These included age, sex, history of drug abuse and smoking and disease duration. The odds ratio (OR) is a measure commonly used in statistics and epidemiology to quantify the strength and direction of the association between two variables, particularly in the context of case-control studies. An odds ratio greater than 1 indicates an increased odds of an event occurring, while an odds ratio less than 1 indicates a decreased odds.

The study has been reviewed and approved by the Institutional Review Board (IRB) and has been found to be in compliance with all relevant ethical guidelines and standards for research involving human participants. All subjects gave informed consent.

RESULTS

A total of 244 patients diagnosed with PD were included, of whom 146 (59.8%) were men and 98 (40.2%). Table 1 shows the sociodemographic data of our patients in more detail.

A total of 35 (14.3%) patients with ICD (ICD-PD) were found; non-ICD group included 209 subjects(85.7%).

When analyzing antiparkinsonian drugs, a higher use of dopamine agonists was found in the ICD group but did not reach statistical significance (p=0.078). More detailed information on drug intake is shown in Table 2.

Regarding smoking habits, no statistically significant differences were found between the ICD-PD and Non-ICD groups (p=0.73).

Regarding the use of alcohol in ICD-PD a statistically significant difference was found (P=0.019).

No statistically significant difference was found between groups regarding age at diagnosis, age at symptom onset, age, diagnostic delay, and levodopa equivalent doses.

A logistic regression using the following variables as independent levodopa intake, MAOIs, dopaminergic agonists, amantadine, gender, alcoholism and smoking was carried out. Presence of ICD was the dependent variable.

Only the variable alcoholism was identified as a risk factor, as can be seen in its P value 0.034, the OR value is 2.551, indicating that patients with alcoholism have a 2.5 times higher risk of developing ICD in comparison to the other group.The 95% confidence interval provides a range of values within which we can be 95% confident that the true odds ratio lies. In this case, the interval spans from 1.07 to 6.070; the interval does not include 1 which suggests statistical significance. Finally, the p-value was 0.034, which is less than 0.05, suggesting that the association between the variables is statistically significant.

The rest of the variables gave us a P value that does not show statistical significance in its association with impulse control disorder. More details are shown in Table 3.

DISCUSSION

The DSM-IV defines ICDs as the inability to resist an impulse, attraction, or temptation to perform an act that ends up being harmful to the individual or their environment. It includes alterations in sexual behavior, pathological gambling, compulsive shopping, bulimic episodes and

compulsive medication consumption [16]. On the other hand the term "impulsivity" describes a pattern of behaviors based on hasty decisions, without considering potential adverse consequences [17].

Traditionally four types of behaviors have been recognized and classified as ICDs; namely hypersexuality, compulsive buying, pathological gambling, and compulsive food intake also known as binge eating disorder [18].

Considering the nature of ICDs it has recently been subdivided into two main processes linked to different neural networks and activated by different experimental paradigms: cognitive impulsivity and motor impulsivity. According to Vales et al., cognitive impulsivity refers to the difficulty in tolerating delays in reinforcement leading to a preference for immediate smaller rewards over larger, delayed rewards. On the other hand, according to Smith et al, motor impulsivity refers to the ability to inhibit an inappropriate response or stop an ongoing inappropriate response [19].

Variables associated with ICDs include a personal or family history of alcohol use disorder or pathological gambling, impulsive or novelty-seeking traits, younger age, and male sex [20]. In some studies, the prognosis of impulse control disorders was better in women than in men [21], early onset of

PD, being single, and having smoked or smoked cigarettes [22]. According to what has been described in the literature on our study population there is a relationship between alcohol and ICD.

Younger patients are more likely to be treated with a dopaminergic agonist; the effect of age was maintained after controlling for dopaminergic agonist exposure [23]; however, in our study such an association was not found.

Chronic dopaminergic treatment can induce motor and non-motor side effects, mainly DIL and CDI. In fact, the incidence of ICD has been increasingly recognized in recent years; it has been suggested that this is probably related to the increased use of dopaminergic agonists [24].

The association of ICDs in PD with treatment with dopamine agonists has been studied and this association depends on the dose and is similar in the entire class of dopamine agonists [25]. In the present study, only a trend was found without reaching a statistically significant difference.

Use of alcohol has been frequently associated with impulse control problems due to hypoactive function and disrupted network connectivity in regions involving the ventromedial prefrontal cortex, caudate and left lateral/dorsolateral prefrontal cortex underlie stress-related impulse control

difficulties in alcohol-dependent patients [26]. Alcohol use was the only statistically significant risk factor found in our study.

ICD is associated with poor quality of life of the patient and their caregivers, as well as delinquent behaviors, so its timely detection and management is important [27]. ICD may also function as a coping strategy for the existential and personal crises that often follow the diagnosis of chronic disease [28]. Screening is not always straightforward in clinical practice as it relies on the self-assessment of PwP who may lack insight into the frequency, severity and consequences of their own behavior [29]; because of this, doctors must carefully evaluate patients with maladaptive behaviors [30].

There are several possible reasons why one study may fail to show an association between age and impulse control disorders, even though other studies have reported such an association. Here are some factors to consider: 1) sample size, if the study with no observed association has a smaller sample size compared to the studies that found an association, it may not have had enough statistical power to detect the effect. In smaller samples random variations can have a more significant impact on the results. 2) Study

design, design and methodology can greatly influence the outcomes. Different studies may use different research designs (cross-sectional, longitudinal, case-control, etc.) and data collection methods which can lead to varying results. 3) Differences in the characteristics of the study populations can play a significant role. If the study with no association focused on a population with unique characteristics or risk factors it may not be directly comparable to other studies. Factors such as cultural, genetic, or socioeconomic differences can influence the prevalence of impulse control disorders; and 4) Random chance, sometimes, even in well-designed studies, results can appear due to random chance. This is more likely to occur in smaller studies but can still happen in larger ones.

An additional factor to consider is the time period. ICD may have varying prevalence rates across different time periods. A study conducted at a particular point in time may not reflect the current state of the population's impulse control disorders, specially when risk factors are already known and accounted for when choosing an antiparkinsonian drug or dose.

Finally, alcohol frequency (number of days per week or per month an individual consumes alcoholic beverages) or alcohol quantity (amount of alcohol consumed on each occasion

expressed in standard drink units) was not assessed. Future studies should include these variables.

CONCLUSION

With this study our objective was to identify the various risk factors for the development of impulse control disorders in the Mexican population. The prevalence of ICD was within the numbers reported in the literature. Nevertheless, among the known risk factors only alcohol use was statistically related to ICDs.

Conflicts of interest

The authors of this manuscript have no conflicts of interest to declare.

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Table 1: Sociodemographic data of the sample between the groups

Variable	ICD-PD		Non-ICD-PD		P
	Mean	Std. deviation	Mean	Std. deviation	
Age	61.51	11.763	63.30	12.171	0.420
Gender	.34	.487	.41	.493	0.445
Disease duration	7.66	4.814	7.33	5.330	0.734
Years of education	12.86	5.359	10.26	5.206	0.011
H&Y	2.20	.719	2.37	.787	0.200
Age of onset of symptoms	52.46	11.840	54.42	13.447	0.418
Age of diagnosis	54.40	11.790	56.37	13.134	0.405

ICD. Impulse control disorder.

485 **Table 2.** Comparison of the main demographic and clinical

486 characteristics between patients with and without ICD.

Variable	ICD-PD (N=35)	Non-ICD-PD (n=189)	p
Male gender	23 (65.7%)	123 (65%)	0.283
Use of amantadine	6 (17.1%)	23 (12.1%)	0.221
Smoking history	10 (28.5%)	54 (28.6%)	0.438
Alcohol intake history	16 (45.7%)	55 (29.1%)	0.019*
Use of levodopa	35 (100%)	189 (100%)	0.175
Use of dopamine agonist	20 (57.1%)	89 (47.1%)	0.078
Use of MAOi	4 (11.4%)	38 (20%)	0.236

487 ICD. Impulse control disorder. PD. Parkinson's disease. MAOi.

488 Monoamine oxidase inhibitor.

489

490 **Table 3.** Comparison of the main demographic and clinical

491 characteristics using logistic regression

Variable	**OR**	**95% Confidence Interval**	**P value**
MAOI	0.488	.154 - 1.549	0.223
Dopaminergic Agonist	1.888	.847 - 4.210	0.120
Amantadine	2.006	.687 - 5.855	0.203

Gender (female)	0.885	.381 - 2.055	0.776
Alcoholism	2.551	1.07 - 6.070	0.034*
Smoking	0.889	.361 - 2.690	0.798
Disease duration	.991	.910 - 1.079	0.838
LEDD	1.000	.999 - 1.000	0.956
Age	0.985	.956 - 1.016	0.350

LEDD. Levodopa equivalent daily dose. MAOi. Monoamine oxidase inhibitor. OR. Odds ratio.