Dopamine Agonist-Induced Impulse Control Disorders in Patients With Prolactinoma: A Cross-Sectional Multicenter Study

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Context: Dopamine agonist (DA)-induced impulse control disorder (ICD) in patients with prolactinomas is not sufficiently known.

Objective: To evaluate the prevalence of DA-induced ICDs and possible risk factors related to these disorders in patients with prolactinoma.

Design, Setting, and Participants: This is a cross-sectional multicenter study involving 308 patients with prolactinoma followed up in tertiary referral centers who received at least three months of DA therapy. DA-induced ICDs (pathological gambling, hypersexuality, compulsive shopping, and compulsive eating) and impulsivity were assessed using the Questionnaire for Impulsive-Compulsive Disorders in Parkinson Disease and the Barratt Impulsiveness Scale-11, respectively. Patients were evaluated in terms of parameters related to ICD development.

ISSN Print 0021-972X ISSN Online 1945-7197
Printed in USA

Received 12 October 2018. Accepted 4 March 2019.
First Published Online 8 March 2019

Abbreviations: BIS-11, Barratt Impulsiveness Scale-11; BRC, bromocriptine; CAB, cabergoline; DA, dopamine agonist; *DSM*, *Diagnostic and Statistical Manual of Mental Disorders*; ICD, impulse control disorder; PD, Parkinson disease; PRL, prolactin; QUIP, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease.

Results: Any ICD prevalence was 17% (n = 51). Hypersexuality was most common (6.5%). Although any ICD and hypersexuality were more common in male patients ($P = 0.009$, $P < 0.001$, respectively), compulsive eating was more common in female patients ($P = 0.046$). Current smoking, alcohol use, and gambling history were more frequent ($P = 0.033$, $P = 0.002$, $P = 0.008$, respectively) in patients with any ICD. In Barratt Impulsiveness Scale-11 total, attentional, motor, and nonplanning scores were higher in patients with any ICD ($P < 0.001$). Current smoking and alcohol use were more frequent ($P = 0.007$, $P = 0.003$, respectively) and percentage increase of testosterone levels at last visit was higher ($P = 0.021$) in male patients with prolactinomas with hypersexuality.

Conclusion: Any ICD may be seen in one of six patients with prolactinoma who are receiving DA therapy. Endocrinology specialists should be aware of this side effect, particularly in male patients with a history of gambling, smoking, or alcohol use. (***J Clin Endocrinol Metab*** **104: 2527–2534, 2019)**

Prolactinomas are the most common tumors among functional pituitary adenomas (1). Galactorrhea, gonadal dysfunction, and the tumoral mass effect are the main symptoms and findings. Primary treatment of prolactinoma is medical treatment with dopamine agonists (DA) (2). Bromocriptine (BRC) and cabergoline (CAB) are widely used ergo-derived DAs. DA therapy normalizes prolactin (PRL) levels in most cases, where gonadal dysfunction and infertility resolves and shrinkage of tumors are detected (3). DAs are generally well tolerated, however, in some cases side effects such as nausea, vomiting, nasal congestion, postural hypotension, dizziness, and syncope occur (4). Rhinorrhea, painless vasospasm, pleural effusion, pulmonary or retroperitoneal fibrosis, insomnia, mood changes, and psychosis may also be seen, whereas increased risk of valvular heart disease is still controversial (4, 5).

Impulse control disorder (ICD) is described as "failure to resist an impulse, drive or temptation to perform an act that is harmful to the person or others" according to the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) (Fourth Edition, Text Revision) criteria (6). Pathological gambling, hypersexuality, compulsive eating, and compulsive shopping included among ICDs in accordance to *DSM*-IV, Text Revision, although they are classified into different categories in *DSM*-V criteria (6, 7). In addition to prolactinomas, DA therapy can also be used in Parkinson disease (PD), which has been associated with ICDs (8–10). Recently, an increase has been observed in case reports demonstrating DA-induced ICDs in patients with prolactinoma, despite the low doses of DA administration in these patients compared with PD (11–19). DA-induced ICD was assessed in a large number of series and meta-analyses in PD (8–10, 20–24), however, there are a limited number of studies in prolactinomas (25–28) and only one of these studies was designed as a case control study (26).

In this multicenter large-scale study, we aimed to evaluate the prevalence of pathological gambling, hypersexuality, compulsive shopping, and compulsive eating and possible factors associated with these disorders in patients with prolactinoma receiving DA therapy, and to increase awareness of this important side effect among endocrinology specialists.

Material and Methods

Participants

This is a cross-sectional multicenter study including patients with prolactinoma (n = 308; 216 females, 92 males) followed in 11 tertiary referral centers. Patients enrolled in the study had been receiving DA therapy for at least three months and were currently under treatment at the time of the study. Patients who had previously received DA therapy but were not currently receiving DA therapy were excluded from the study. All patients were evaluated and followed by experienced endocrinologists. The diagnosis of prolactinoma was confirmed according to the typical clinical signs and symptoms, radiologic findings (pituitary adenoma confirmed by MRI), and laboratory tests (high PRL levels in at least two different blood samples) with respect to the current guideline (2). Inclusion criteria consisted of prolactinoma diagnosis of patients with a baseline pituitary adenoma size $\geq$5 mm and baseline PRL level >100 ng/mL. Patients with other secondary hyperprolactinemia etiologies were excluded from the study. Patients with psychiatric disorders or who were unable to complete the required questionnaires were not included in this study.

Written informed consent was obtained from participants and the study was approved by the Clinical Ethics Committee of Bakirkoy Dr. Sadi Konuk Training and Research Hospital (2018/44). The study was performed in accordance with the Helsinki recommendations.

ICD screening tests and measures of impulsivity

DA-induced ICDs were assessed using the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP) form (29). QUIP has three sections and section 1 (ICD section) was used to evaluate pathological gambling, hypersexuality, compulsive shopping, and compulsive eating in our patients.

The QUIP section 1 consists of five questions including introductory questions that define and provide examples of behavioral problems. The patients were questioned regarding whether they started to have behavioral changes at any time after the onset of DA therapy. Because each patient was assessed in different tertiary referral centers, the final evaluation of the

questionnaires was made by two experienced psychiatry specialists (C.U. and O.M.) through objective criteria and cutoff points based on the validation of the QUIP study by Weintraub *et al.* (29).

Barratt Impulsiveness Scale-11 (BIS-11) (30) was also applied and the validity and reliability of this questionnaire in Turkey was previously reported by Gulec *et al.* (31). The BIS-11 is a 30-item self-report questionnaire designed to measure impulsiveness. All items are scaled on a 4-point Likert scale (1 = rarely/never; 2 = occasionally; 3 = often; 4 = almost, always). The factor analyses revealed 3 components as follows: (i) attentional impulsiveness (inability to focus attention or concentrate), (ii) motor impulsiveness (acting without thinking), and (iii) nonplanning impulsiveness (lack of forethought).

Study design and procedures

QUIP and BIS-11 were performed after the patients were instructed in detail on how to perform the tests by endocrinologists in each center. All psychiatric evaluations were stored and then evaluated by two experienced psychiatrists who were blinded to patients' endocrinological information.

The frequencies of each type of ICD and those with more than one ICD were evaluated; these frequencies were compared by sex. The possible factors related to ICD development were recorded by endocrinologists at each center. Patients with and without any ICD were compared according to age at diagnosis, sex, education, marital status, current smoking, alcohol use, gambling history, maximal tumor diameter, baseline PRL levels, duration of DA therapy, maximum-maintenance and CAB cumulative doses (number of patients receiving BRC was inadequate to compare in the study group), nadir PRL levels, and residual tumor diameter at last visit. CAB cumulative dose was calculated according to follow-up period or time of ICD onset after the initiation of CAB in patients without any ICD and patients with any ICD, respectively. BIS-11 scores (total, attentional, motor, and nonplanning scores) were compared between groups and cutoff scores related to ICD were determined in these patients. Dopa-testotoxicosis, which was previously defined by De Sousa *et al.* (18), was evaluated in terms of possible risk factors in male patients with and without hypersexuality.

Statistical analyses were performed using SPSS version 21.0 (IBM, Armonk, NY). Categorical variables were defined by frequency and percentage rate, and numerical variables were defined by mean ± SD. In dual independent group comparisons, Student *t* test was used for normally distributed numeric variables, and the Mann-Whitney *U* test was used for nonnormally distributed data. Categorical variables were compared using the χ^2 test. Statistically significant results were defined as $P < 0.05$. Predictors of ICD development were assessed by a multivariate binary logistic regression analysis. Variables that have a $P < 0.05$ in univariate analysis were included in the multivariate analysis model. Cutoff thresholds for BIS-11 scores were analyzed by receiver operating characteristic curves. Sensitivity and specificity calculations were made to determine the power of the BIS-11 scores.

Results

The mean age of the patients was 36 ± 12 years (range, 14 to 72 years). The prevalence of ICD was 17% (n = 51) in the study population. The distribution of ICD was as follows; only hypersexuality (6.5%, n = 20), only pathological gambling (0.6%, n = 2), only compulsive shopping (1%, n = 3), only compulsive eating (2.9%, n = 9), and presence of more than one ICD (5.5%; 13 patients with double ICD, 3 patients with triple ICD, 1 patient with quadruple ICD). When patients with more than one ICD are distributed, frequencies were determined as hypersexuality (9.7%, n = 30), pathological gambling (2.9%, n = 9), compulsive shopping (4.5%, n = 14), or pathological eating (6.1%, n = 19). In patients who were receiving CAB maintenance therapy, 17% had at least one ICD (50/289 patients). Compulsive shopping only developed in 1 of 19 patients (5%) who was receiving BRC maintenance therapy. The mean age for onset of any ICD was 34 ± 10 years, the mean time for onset of any ICD was 28 ± 31 months. The frequency of ICD was found to be 35% in patients with a follow-up period ≤12 months (26/74 patients), whereas the frequency of ICD was found to be 11% in patients with a follow-up period >12 months (25/ 234 patients).

In gender comparisons, whereas both any ICD and hypersexuality were more common in male patients ($P = 0.009$, $P < 0.001$, respectively), compulsive eating was more common in female patients ($P = 0.046$). Comparison of frequencies of ICDs by sex is shown in Table 1.

In patients with any ICD, current smoking, alcohol use, and gambling history were more frequent ($P = 0.033$, $P = 0.002$, and $P = 0.008$, respectively) and baseline PRL levels and nadir PRL levels at last visit were higher ($P = 0.015$ and $P = 0.031$, respectively) (Table 2). In logistic regression analysis nadir PRL levels at last visit ($P = 0.042$; OR = 1.005; 95% CI = 1.000 to 1.010), male sex ($P = 0.015$; OR = 2.427; 95% CI = 1.188 to 4.959), and alcohol use ($P = 0.01$; OR = 4.208; 95% CI = 1.412 to 12.541) persisted as independent risk factors. Baseline PRL levels, current smoking, and gambling history were no longer important in the risk assessment.

BIS-11 total, attentional, motor, and nonplanning scores were higher in patient with ICD ($P < 0.001$). The optimum cutoff thresholds of attentional score = 15 [95% CI; sensitivity of 65% (50% to78%) and specificity of 84% (79% to 88%)], motor score = 19 [95% CI; sensitivity of 63% (48% to 76%) and specificity of 84% (79% to 88%)], nonplanning score = 26 [95% CI; sensitivity of 57% (42% to 71%) and specificity of 90% (86%–94%)], total score = 61 [95% CI; sensitivity of 56% (83% to 98%) and specificity of 98% (97% to 99%)]. Overall these scores were associated with any ICD.

In male patients with hypersexuality, current smoking and alcohol use were more common ($P = 0.007$ and $P = 0.003$, respectively). Although CAB maintenance dose tended to be higher in male patients with hypersexuality, there was no statistical significance ($P = 0.09$). The percentage increase of testosterone levels at last visit was higher in those with hypersexuality ($P = 0.021$)

Table 1. Comparison of ICD Frequencies According to Sex

N = 308	Female Patients With Prolactinomas (n = 216)	Male Patients With Prolactinomas (n = 92)	*P*
Any ICD, n; %	28 (10)	23 (25)	**0.009**
Only pathological gambling, n; %	1 (0.9)	1 (1.1)	NS
Only hypersexuality, n; %	7 (3.2)	13 (14)	**<0.001**
Only compulsive shopping, n; %	1 (0.9)	2 (2.2)	NS
Only compulsive eating, n; %	9 (4.2)	0	**0.046**
More than one ICD, n; %	10 (4.6)	7 (7.6)	NS

$P < 0.05$ statistically significant. Significant *P* values are shown in bold

Abbreviation: NS, not significant.

(Table 3). Logistic regression analysis revealed that alcohol use and current smoking were the independent risk factors in the development of hypersexuality ($P = 0.044$; OR = 5.208; 95% CI = 1.045 to 25.954 and $P = 0.042$; OR = 3.071; 95% CI = 1.040 to 9.069, respectively). The percentage increase of testosterone levels was no longer important in the risk assessment.

Discussion

In this study, the prevalence of DA-induced ICDs in our patients with prolactinoma was 17%. In the literature, frequencies were reported as ~8% to 25%, however, these studies were performed with few patients or in a study that was also conducted via electronic surveys (25, 26, 28). In our study, the patient cohort was larger, and a patient-based evaluation form was used instead of online questionnaires. In a current meta-analysis, DA-induced ICD was reported between 2.6% and 34.8% in PD (9). Serious adverse drug event reports by the US Food and Drug Administration report that 710 DA-induced ICD events in the last 13 years were related to PD, restless leg syndrome , and prolactinoma affecting 62%, 24%, and 3.5% of the patients, respectively (32). The high incidences in PD and restless leg syndrome may possibly be related to higher doses of DA therapy and the use of increased affinity for cerebral D3 receptor drugs such as pramipeksol and ropinirol. D3 receptors are localized in

Table 2. Comparison of Patients with Prolactinoma With and Without Any ICD in Terms of Demographic, Clinical, Laboratory Findings, and BIS-11 Scores

N = 308	Patients Without Any ICD (n = 257)	Patients With Any ICD (n = 51)	*P*
Age at diagnosis, y, mean ± SD	36 ± 12	35 ± 13	NS
Education, y, mean ± SD	8.8 ± 3.9	9.3 ± 3.9	NS
Marital status, n; % married	198 (77)	33 (64)	NS
Current smoking, n; %	55 (21)	18 (35)	**0.033**
Alcohol use, n; %	9 (4)	7 (14)	**0.002**
Gambling history, n; %	2 (0.7)	3 (6)	**0.008**
Maximum tumor diameter, mm, mean ± SD	14.6 ± 11.2	16.7 ± 11.7	NS
Baseline PRL levels, ng/mL, mean ± SD	793 ± 1743	1062 ± 1705	**0.015**
Duration of DA therapy, mo, mean ± SD	50 ± 44	49 ± 39	NS
CAB maximum dose, mg/wk, mean ± SD	1.2 ± 0.7	1.5 ± 1.1	NS
CAB maintenance dose, mg/wk, mean ± SD	0.7 ± 0.4	1.5 ± 1.1	NS
BRC maximum dose, mg/d, mean ± SD	6.2 ± 3.5	—	—
BRC maintenance dose, mg/d, mean ± SD	5.5 ± 3.8	—	—
CAB cumulative dose, mg,[a] mean ± SD	165 ± 174	172 ± 237	NS
BRC cumulative dose, mg, mean ± SD	8310 ± 8168	—	—
Nadir PRL levels at last visit, ng/mL, mean ±SD	22 ± 41	41 ± 91	**0.031**
Residue tumor diameter at last[a] visit, mm, mean ± SD	6.6 ± 6.9	7.4 ± 6.7	NS
BIS-11 questionnaire, mean ± SD			
Total score	52 ± 6	65 ± 8	**<0.001**
Attentional score	13 ± 2.5	17 ± 3.3	**<0.001**
Motor score	16 ± 2.7	21 ± 3.7	**<0.001**
Nonplanning score	22 ± 3.6	27 ± 4.3	**<0.001**

$P < 0.05$ statistically significant. Significant *P* values are shown in bold.

Abbreviation: NS, not significant.

[a]CAB cumulative dose was calculated according to follow-up period or time of ICD onset after the initiation of CAB, in patients without any ICD and patients with ICD, respectively.

Table 3. Comparison of Male Patients With Prolactinoma With and Without Hypersexuality in Terms of Demographic, Clinical, and Laboratory Findings

N = 92	Male Patients Without Hypersexuality (n = 72)	Male Patients With Hypersexuality (n = 20)	*P*
Age at diagnosis, y, mean ± SD	44 ± 14	40 ± 10	NS
Education, y, mean ± SD	8.3 ± 3.3	9 ± 3.8	NS
Marital status, n; % married	59 (82)	15 (75)	NS
Current smoking, n; %	20 (28)	12 (60)	**0.007**
Alcohol use, n; %	3 (4)	5 (25)	**0.003**
Maximum tumor diameter, mm, mean ± SD	26 ± 14	25 ± 13	NS
Baseline PRL levels, ng/mL, mean ± SD	2158 ± 2931	1739 ± 1929	NS
Baseline testosterone levels, nmol/L, mean ± SD	4.3 ± 4.1	4.9 ± 4.8	NS
Presence of hypogonadism at initial visit, n; %	63 (88)	17 (85)	NS
Duration of DA therapy, mo, mean ± SD	54 ± 40	46 ± 41	NS
CAB maintenance dose, mg/wk, mean ± SD	0.7 ± 0.5	1.7 ± 1	NS
CAB cumulative dose, mg,[a] mean ± SD	227 ± 228	226 ± 231	NS
Nadir PRL levels at last visit, ng/mL, mean ± SD	21 ± 57	14 ± 13	NS
Residue tumor diameter at last visit, mm, mean ± SD	10 ± 9.7	11 ± 8.5	NS
The highest testosterone levels at follow-up period, nmol/L, mean ± SD	12.4 ± 5.7	13.7 ± 8.5	NS
Percentage increase of testosterone levels at last visit, %mean ± SD	387 ± 719	471 ± 504	**0.021**
Presence of hypogonadism at last visit, n; %	28 (39)	8 (40)	NS
Androgen replacement therapy at last visit, n; %	15 (20)	3 (15)	NS

$P < 0.05$ statistically significant. Significant *P* values are shown in bold.

Abbreviation: NS, not significant.

[a] CAB cumulative dose was calculated according to follow up period and time of hypersexuality onset, in male patients without hypersexuality group and male patients with hypersexuality group, respectively.

the mesocorticolimbic pathway, which is associated with reward, novelty, and risk assessment mechanisms (33). Although BRC and CAB are primarily effective on D2 receptors, they may also affect D3 receptors and cause DA-induced ICD (34).

The most common ICD component in our study was hypersexuality, which was compatible with studies by Bancos *et al.* (26) and Celik *et al.* (28) that investigated DA-induced ICDs in prolactinomas. Also, in a recent meta-analysis, hypersexuality was found to be the most common ICD in patients with PD (10). In our series, pathological gambling was the least common ICD, however, it is commonly reported in both patients with PD and patients with prolactinoma with ICD (9, 12–17, 24, 25). We attributed the low frequency of pathological gambling in our study to the prohibition of gambling in our country; the gambling history frequency of 1.6% in all of our series is already quite low. The second most common ICD in our study was compulsive eating. Although compulsive eating is frequently reported in patients with PD (9, 10), it is accepted as the ICD component with lowest positive predictive value in the QUIP test (29). This is explained by the difficulty in distinguishing pathological and excessive eating behaviors.

When the frequency of ICD components was compared according to sex, hypersexuality and compulsive eating were more common in males and females, respectively. Whereas there is no comparison in this aspect in the literature, male sex has been reported to be a risk factor for ICD development in both patients with PD and patients with prolactinoma, which is similar to our results (9, 26). In our cohort, male sex has increased ICD risk by 2.4 times and was an important independent risk factor.

Apart from male sex, a number of risk factors have been associated with the development of DA-induced ICD, such as younger age, history of psychiatric symptoms, being single, smoking, alcohol use, and especially gambling history for compulsive gambling (9, 24). In this study, current smoking, alcohol, and gambling history were higher in those with any ICD, and alcohol use was the most important independent risk predictor. History of higher depression-anxiety symptoms or presence of psychiatric disorders have been previously reported as risk factors (35, 36). However, in this study, we excluded patients with diagnosis of psychiatric disorders.

DA with higher D3 receptor affinity is related to increased ICD development and higher dose of DA therapy is also reported as important in patients with PD with ICD (9, 21, 37). In prolactinomas, Bancos *et al.* (26) reported that the DA dose was not effective in the ICD development. Conversely, Barake *et al.* (27) reported that CAB dose was associated with increased impulsivity. In our study, even though the CAB maintenance dose was higher in patients with any ICD, the difference did not reach statistical significance. It was deduced from our

clinical experience that patients' symptoms were relieved by reducing the CAB dose, which is supported by case reports in the literature, highlighting the importance of DA dose in ICD development (16, 17, 25). Therefore, it is crucial to continue the treatment with the lowest dose of DA therapy that provides normoprolactinemia in patients with prolactinoma.

It was interesting to detect higher baseline and last-visit PRL levels in patients with any ICD in our cohort. This might be because of the higher number of male patients in the ICD group, who have higher PRL levels caused by higher frequency of macroprolactinomas (38). However, it has been reported that independent from DA therapy, the disease itself is a risk factor for ICD in patients with PD (24). The same concept may apply to prolactinomas. In our literature review, we did not find any clear evidence of hyperprolactinemia associated with ICD development or increased impulsivity. However, the answer to this question may only be investigated in comparative studies conducted with a control group and patients with prolactinoma before initiation of DA treatment.

In the literature, genetic analysis was investigated in patients with PD who developed ICD. Dopamine receptor D3, dopamine transporter, tryptophan hydroxylase type 2, and some other gene polymorphisms were found to be associated with an increased risk of developing ICDs in patients with PD (9). In prolactinomas, polymorphisms of the drug transporter gene *ABCB1* have been associated with the occurrence of central side effects (39), but this polymorphism could not be demonstrated in a patient with prolactinoma with DA-induced ICD (19). The genetic basis of ICD development in patients with prolactinomas needs to be determined.

Impulsivity can be defined as a tendency to act with nonplanned and excessive behavior against internal or external stimuli, which is characterized by little or no forethought and reflection, ignoring the negative consequences that may occur (40). BIS-11, one of the most important scales used for evaluating impulsivity, is frequently used in the evaluation of DA-induced ICD in PD and has been previously used in two studies with prolactinoma that had a smaller sample compared with our study (27, 28). One of the two studies found increased attentional scores in hyperprolactinemic patients on DA therapy (27), but these findings were not supported in the other study (28). In our large cohort, we found that total, attentional, motor, and nonplanning scores were quite high in patients with any ICD showing increased impulsivity. BIS-11, which is usually used as a standardization for studies rather than a single diagnostic marker, is actually a high-throughput method for screening patients in outpatient settings. However, because this method lacks cutoff levels, we investigated cutoff levels related to increased impulsivity. Referral to psychiatric counseling may be appropriate for patients with scores higher than the scores obtained from these tests, which can be easily applied in outpatient settings.

One of the aims of this study was to evaluate the dopatestotoxicosis hypothesis of De Sousa *et al.* (18). According to the hypothesis, relative rapid onset of eugonadism with DA therapy after prolonged hypogonadism was suggested to be associated with hypersexuality. To assess this hypothesis, we compared the percentage increase of testosterone levels from baseline and found that it was higher in male patients with hypersexuality. De Sousa *et al.* (18) reported that the first six months are important in the development of hypersexuality. Even though ICD developed in the first year in most of our patients, we also observed that this period could take as long as 2.5 years. Therefore, percentage increase of testosterone levels was more important than the time period. However, the time of ICD onset would be better established by a prospective study. In contrast to De Sousa *et al.* (18), Bancos *et al.* (41) suggest that as DA-induced ICD is not limited to male patients; it is difficult to accept this hypothesis as a major factor in hypersexuality development. We agree with this opinion because of the evidence of DA-induced hypersexuality in female patients (12, 16, 17, 28). There are no data on whether estradiol levels are related to DA-induced hypersexuality in female patients. It is also difficult to evaluate the effect of estradiol levels on hypersexuality, because estradiol levels vary according to menstrual cycle phases. Therefore, we could not evaluate serum estradiol levels in our female patients with prolactinoma. Current smoking and alcohol use, which were found as contributing factors in our study, may also be effective in this entity.

Although we do not have a control group in our study, the data obtained with the comparison of a sufficient number of patients, especially those with and without any ICD, reduces this limitation of our study. Another limitation of our study is that QUIP is intended to evaluate PD. However, we used questions from the ICD section in QUIP to perform a general evaluation of ICD symptoms. Therefore, questions not specific to PD were chosen in our evaluations. In addition, the tests of all patients were evaluated by two psychiatrists experienced with ICD at the same department to eliminate the heterogeneity of test results. In our series, we used QUIP with good eligibility and our study may be a pioneer leading to the future validation of this questionnaire in the evaluation of ICD in patients with prolactinoma. The personal approach of endocrinology specialists in the management of patients with DA-induced ICD and its effect on long-term follow-up and assessment of repeated

questionnaires are also planned to be evaluated in a future study.

In conclusion, DA-induced ICD may develop in one of six patients with prolactinoma who are receiving DA therapy. Endocrinology specialists should be aware of this side effect, especially in male patients with history of gambling, smoking, and alcohol use. Close monitoring is required at the initial visit and during the follow-up period because early identification of DA-induced ICDs is important. QUIP and BIS-11 tests can be used to screen the increased impulsivity in DA-induced ICD. A multidisciplinary approach including psychiatric evaluation in patients at risk is essential to prevent undesirable consequences.

Acknowledgments

The authors greatly appreciate the efforts of Assistant Professor Feyza Nur Tuncer (Istanbul University Aziz Sancar Institute of Experimental Medicine, Department of Genetics) in the language editing of this paper.

Financial Support: This research did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

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Disclosure Summary: The authors have nothing to disclose.

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