



# Recent Perspectives on Impulse Control Disorder in Dopamine Agonist-Treated Patients in Endocrine Practice

Khaled M. Aldahmani<sup>1,2</sup> Mussa H. AlMalki<sup>3,4</sup>

<sup>1</sup>Division of Endocrinology, Tawam Hospital, SEHA, Al Ain, Abu Dhabi, United Arab Emirates

<sup>2</sup>Department of Medicine, College of Medicine and Health Sciences, United Arab Emirates University, Al Ain, Abu Dhabi, United Arab Emirates

<sup>3</sup>Department of Endocrinology, Obesity, Endocrine, and Metabolism Center, King Fahad Medical City, Riyadh, Saudi Arabia

<sup>4</sup>College of Medicine, Alfaisal University, Riyadh, Saudi Arabia

**Address for correspondence** Khaled Aldahmani, MBBS, FRCPC, Division of Endocrinology, Tawam Hospital, Al-Ain, Abu Dhabi, United Arab Emirates (e-mail: kmdahmani@seha.ae).

J Diabetes Endocrine Practice 2024;7:112–117.

## Abstract

### Keywords

- ▶ pituitary
- ▶ dopamine agonist therapy
- ▶ impulse control disorder
- ▶ prolactinoma
- ▶ hyperprolactinemia

Dopamine agonists (DAs) are the primary treatment for patients with hyperprolactinemia. However, there are potential risks of impulse control disorders (ICDs), particularly in those with predisposing factors. Early recognition of ICDs is essential, as reducing the dose or discontinuing the medication often resolves the issue. In some cases, alternative treatments like surgery may be necessary, especially for microprolactinoma or intrasellar macroprolactinoma. Future research should focus on identifying confounding risk factors for ICD development, confirming the presence of ICDs with the help of psychiatrists, documenting the severity of ICDs, and providing guidance on optimal management strategies upon detection of ICDs. We here briefly review the frequencies, risk factors and provide practical guidance on identification and management of ICDs in the context of managing pituitary disorders.

## Introduction

Pituitary adenomas (PAs) are frequently encountered in clinical practice, with an estimated prevalence of ~1 in 1,000 persons.<sup>1</sup> Prolactinomas and nonfunctioning pituitary adenomas (NFPAs) are the predominant types of PAs.<sup>2</sup> Prolactinoma exhibits a higher prevalence in women; nearly half of all adenomas are more than 1 cm in size.<sup>1,2</sup>

Unlike other PAs, prolactinomas are very sensitive to dopamine agonist (DA) therapy (such as cabergoline and

bromocriptine), resulting in the normalization of prolactin levels, reduction in tumor size, and improvement in vision.<sup>3</sup> Although these drugs are typically well tolerated, DA treatment can be linked to undesirable effects. The most common adverse effects of DA therapy are nausea, vomiting, dizziness, headache, and orthostatic hypotension.<sup>4</sup> These are usually managed with dose reduction, gradual titration, or by taking the tablet with a small snack at night. However, there are other less common but more serious side effects associated with DA use, such as valvular heart disease and impulse control disorders (ICDs).<sup>4</sup>

article published online  
July 29, 2024

DOI <https://doi.org/10.1055/s-0044-1787693>.  
ISSN 2772-7653.

© 2024. Gulf Association of Endocrinology and Diabetes (GAED). All rights reserved.

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (<https://creativecommons.org/licenses/by-nc-nd/4.0/>)

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

The correlation between the emergence of ICD in patients undergoing DA treatment is firmly established in individuals with Parkinson's disease.<sup>5</sup> Within this specific category of patients, DAs are commonly administered in large doses and for extended periods, accumulating high doses over time.<sup>5</sup>

### Impulse Control Disorder and Dopamine Agonist Therapy

—Fig. 1 illustrates the growing acknowledgment of an association between ICDs and DA in the medical literature. However, only a minority were detected when pituitary was used as an extra search term.<sup>6</sup> The association between ICDs and DA therapy is relatively new in pituitary medicine, with studies documenting a widely variable frequency ranging between 0 and 61% of patients on DA therapy.<sup>7</sup>

A recent cross-sectional study used questionnaires of 200 patients (52.5% female, 69.5% married) diagnosed with PAs (93.5% prolactinomas and 6.5% NFPAs) in four referral centers in the Kingdom of Saudi Arabia and the United Arab Emirates.<sup>7</sup> The majority of patients (87%) were treated with cabergoline. The findings indicate that nearly half (52%) of the participants reported experiencing symptoms of ICD. In the context of multivariate analysis, it was found that being young and having a personal history of psychiatric problems were predictive factors for the occurrence of ICDs, but being single was found to have a protective effect.

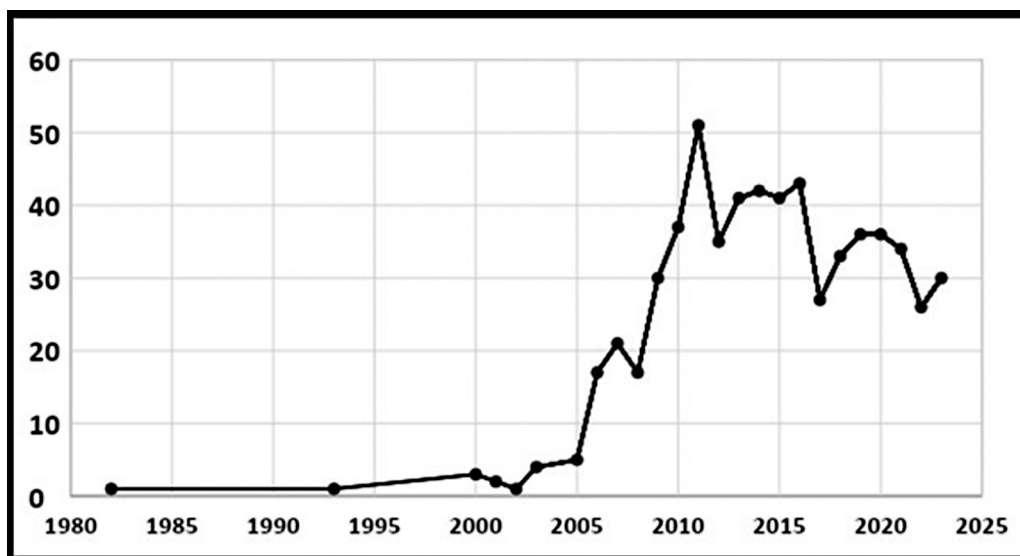
—Fig. 2 illustrates the notably wide distribution in the observed frequency of ICDs across various published studies involving patients with PAs/disorders undergoing DA therapy.<sup>8–19</sup> This variation can be attributed to many factors, as demonstrated in —Table 1.<sup>7–19</sup> These factors include disparities in study demographics (patients with prolactinomas vs. other adenomas or pituitary disorders), sex distribution, study methodologies (cross-sectional vs. prospective designs), the inclusion or exclusion of well-matched control groups, and nuances in DA therapy (type,

duration, dosage, current or prior usage, cumulative dosage).<sup>6</sup> Furthermore, variations in assessment tools (both in quantity and type), whether assessments were self-reported or conducted by health care professionals or experts in ICDs and the presence of additional risk factors for ICD development (smoking, alcohol consumption, history of depression/mental illness, and family predisposition to mental health conditions) can all contribute to the frequency of ICD.<sup>6</sup>

Two important findings from these studies deserve further attention. First, the predominant reliance on self-reported data for diagnosing ICD, including our study, may lead to an overestimation of its frequency not only in patients on DA therapy but also in the healthy control groups. Of note, in the study by Ozkaya et al, the reported frequency of ICD in 40 patients with prolactinomas was 62.5% when based on patient self-reports using Minnesota impulse disorders interview-Revised, but significantly reduced to 15% following an interview with a physician and finally dropped to 7.5% following assessment with a specialized psychiatrist.<sup>15</sup> The same pattern with a 42.5% reduction in frequency was observed in the other group of patients with acromegaly, and none of the 18% patients with NFA was confirmed to have ICD following assessment with a specialized psychiatrist.<sup>15</sup> Hence, while the ICD assessment tool serves well for screening, definitive diagnosis and confirmation necessitate expert involvement. Second, most published studies did not characterize the severity of ICD, its impact on the patient's personal or professional life, and its associated financial, social, and legal consequences.<sup>6</sup>

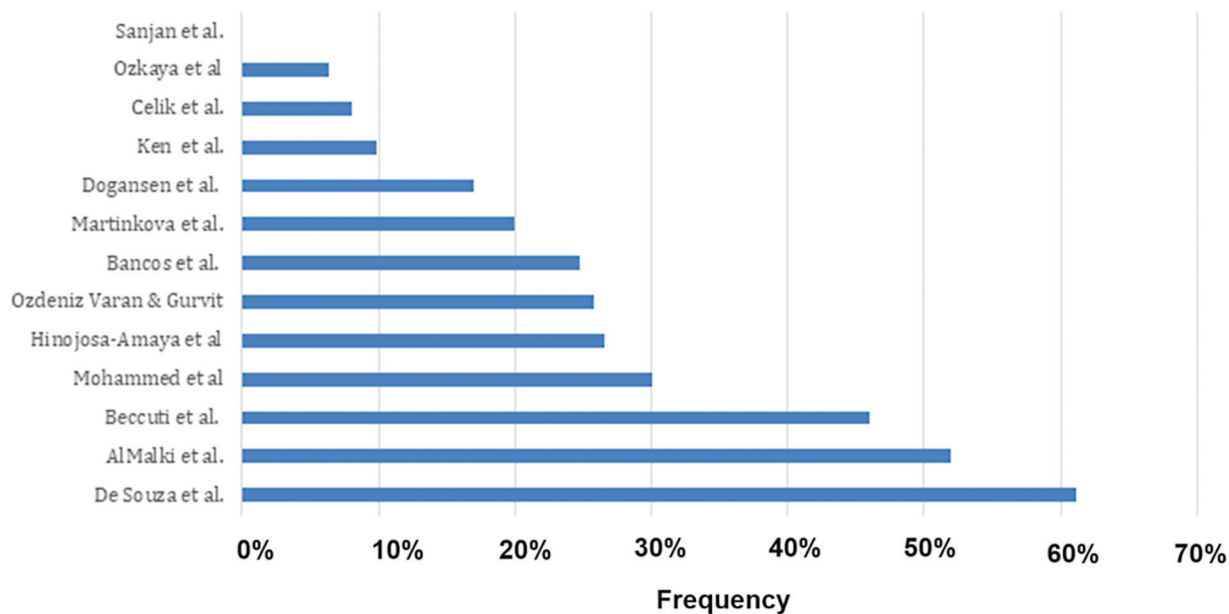
### Implications for Endocrine Practice

Due to its efficacy, tolerability, availability, and affordability, DA remains the first line of treatment in most patients with prolactinoma. Nonetheless, the emerging data about ICDs associated with DA use warrant proper assessment, and weighing the risks and benefits of each treatment modality



**Fig. 1** The increasingly recognized association between impulse control disorder and dopamine agonists as seen by the number of records in the PubMed database between 1982 and 2023. Courtesy of Dr Salem A Beshyah, Abu Dhabi, United Arab Emirates).

## Frequency of ICDs in patients with pituitary disorders on DA therapy



**Fig. 2** The wide distribution of the incidence of impulse control disorders (ICDs) in pituitary-related use of dopamine agonist (DA) therapy.

becomes critical. Before commencing DA therapy, it is essential to educate patients and their families about possible behavioral adverse effects linked to these medications.<sup>21</sup> In selected cases of microprolactinoma, exploring alternative options for surveillance or management with non-DA pharmacological therapy, such as oral contraceptive pills, could be considered. Additionally, when pregnancy is not planned shortly and when expert pituitary surgeons are available, surgery may emerge as a favorable treatment choice, particularly as it can offer a potential cure. Surgery's broader acceptance now positions it as a viable first-line therapy for patients with microprolactinoma and intrasellar macroprolactinoma, as highlighted in a recent consensus statement.<sup>22</sup> This consideration might be particularly important in patients with mental illness or predisposing factors for ICDs. Nevertheless, it is essential to consider the possibility of patients encountering enduring surgical complications, especially if an experienced neurosurgeon does not perform the procedure. Therefore, engaging in comprehensive discussions with the patient and the multidisciplinary team (MDT) is essential for informed decision-making.

During follow-up visits, it is advisable to routinely inquire from the patient and accompanying relatives about symptoms of ICDs and related behaviors.<sup>20</sup> Periodic administration (once or twice yearly) of one of the impulsivity questionnaires utilized in the literature is recommended. Upon the emergence of ICD symptoms, it becomes paramount to assess their severity and societal impact through open discussion thoroughly. Treating physicians should contemplate dose reduction or discontinuation of DA therapy in line with recent consensus management statements and positive outcomes reported in the literature.<sup>22</sup>

Furthermore, a psychiatrist experienced in ICD management is crucial for comprehensive assessment and support. Decision-making regarding the discontinuation of DA treatment should weigh the benefits against the potential risks of relapsing hyperprolactinemia or tumor enlargement upon DA withdrawal.<sup>23–25</sup> Prior to discontinuation, alternative approaches such as pituitary surgery, radiation therapy, or nonpharmacological interventions such as psychotherapy and cognitive behavioral therapy should be considered, ideally in an MDT setting. Regular follow-up and evaluation to document and monitor improvements or resolution of ICDs are essential. ►**Table 2** outlines a practical approach for identifying and managing ICDs in patients undergoing DA therapy.

### Conclusion

DA stands as the primary treatment for patients with prolactinoma and hyperprolactinemia. Nevertheless, it is crucial to be aware of the potential risks of ICDs, particularly in those with predisposing factors. Early recognition is paramount, and dose reduction or medication discontinuation often resolves the issue. In certain cases, it may be required to consider a different approach, such as surgery, particularly when dealing with microprolactinoma or intrasellar macroprolactinoma and when an experienced pituitary neurosurgeon is available.

Future studies should address confounding risk factors associated with ICD development, ensuring confirmation of ICD presence by psychiatrists, documenting the severity of ICD, and providing guidance on optimal management strategies upon ICD detection.

**Table 1** Summary of the studies on impulse control disorder and pituitary-related dopamine agonist therapy

Authors (Ref.)	Year	Region	Study type	Sample size	Frequency <sup>a</sup>	Cohort details	Limitations	Comments
AlMalki et al <sup>8</sup>	2024	KSA and UAE	Cross-sectional survey	200	52%	93.5% PRLoma 6.5% NFA	No control group Not all ICD Rf's assessed	Rf's: FHx or personal Hx of psychiatric illness, younger age
Bancos et al <sup>7</sup>	2014	United States	Cross-sectional survey	77	24.7% PRL 17.1% NFA	77 PRLoma 70 NFA	A small number of patients	
Celik et al <sup>9</sup>	2018	Turkey	Prospective	25	8%	25 PRLoma 32 NFA 32 controls	Small cohort, short-term FU (1 y). Patients with a Hx of current ICD or major psychiatric disorders were excluded; 29% (10/35) of DA Rx patients dropped out	ICD Dx made by an expert physician. ICD reversed or decreased with d/c DA
Dogansen et al <sup>10</sup>	2019	Turkey	Cross-sectional multicenter survey	308	17%	PRLoma on DA Rx for at least 3 mo	No control group	Rf's: current smoking, ETOH, gambling
Hinojosa-Amaya et al <sup>11</sup>	2020	United States	Cross-sectional single-center survey	76	26.5% in DA + ; 23.1% in controls	76 PAs (73 PRLoma)	Small cohort excluded patients with depression and psychiatric illness	
De Souza et al <sup>12</sup>	2020	Australia	Cross-sectional multicenter survey	113	61.1%	113 (95% PRLoma) 99 control	High rate of unemployment, retirement, and smoking c/t control group	42% of ICD in controls Male sex, psychiatry comorbidity, age, Hardy tumor classification, hypogonadism 37% are only aware of ICD risk with DA
Beccuti et al <sup>13</sup>	2021	Italy	Cross-sectional, single-center survey; QUIP	132	46% DA+ 24% DA-	132 patients on DA 58, no DA	Heterogenous cohort (functional hyperPRL and PAs). Excluded patients with psychiatric illnesses; 81% current use of DA	DA use, age, male, hypersexuality; dose and duration, not Rf; increased risk in the elderly; DA increased risk by two-three folds; high baseline risk of ICD in nonexposed cohort
Ozdeniz Varan and Gurvit <sup>19</sup>	2023	Turkey	cross sectional, multicenter	31	25.8% DA+ 15% DA- 16.7% controls	31 PRLoma DA + 20 PRLoma DA - 30 controls	Excluded patients with Rf's for ICDs	No significant difference in ICD prevalence among DA Rx patients
Sanjan et al <sup>14</sup>	2023	India	Prospective, single-center questionnaire	15	0% (incidence)	15 PRLoma (Macro) 15 NFA	Small cohort, short FU(3 mo), excluded patients with Hx of psychiatric disorders, single center	No patients developed ICD, but the impulsivity score increased in the DA-treated patient's c/t baseline
Ozkaya et al <sup>15</sup>	2020	Turkey	Cross-sectional questionnaire interview	80	6.3% (all) 7.5% PRLoma; 5% ACRO	40 ACRO 40 PRLoma 38 NFA 32 controls	Single center	All patients' symptoms resolved after DA discontinuation; ICD with self-report > psychiatrist assessment
Martinkova et al <sup>16</sup>	2011	Slovakia	Retrospective, single-center, structured interview focused on ICDs	20	20%	18 PRLoma	Small study No controls	Dx made by expert Compulsive eating developed in one patient in addition to pathologic gambling Switching to other DAs did not help
Ke et al <sup>17</sup>	2022	China		51				No information about other ICD Rf's

(Continued)

**Table 1** (Continued)

Authors (Ref.)	Year	Region	Study type	Sample size	Frequency <sup>a</sup>	Cohort details	Limitations	Comments
Mohammad et al <sup>18</sup>	2024	Iraq	Cross-sectional, single-center interview (QUIP)	30	9.8% PRLoma DA +; 16.7% PRLoma DA-; 9.1% controls	51 PRL on DA+ 12 PRL on DA- 33 controls	Small study Excluded patients with mental illness	No data about other ICD RFs, like smoking

Abbreviations: ACRO, acromegaly; CAB, cabergoline; c/t, compared to; DA, dopamine agonist; DA +, DA treated; DA-, DA untreated; Dc, discontinue; Dx, diagnosis; ETOH, ethanol; FHx, family history; FU, follow-up; PRLoma, prolactinoma; Hx, history; ICD, impulse control disorder; KSA, Kingdom of Saudi Arabia; NFA, nonfunction adenoma; PAs, pituitary adenomas; QUIP, questionnaire for impulsive-compulsive disorders in Parkinson's disease; RFs, risk factors; Rx, ; UAE, United Arab Emirates.

<sup>a</sup>For the whole sample and subgroups when relevant.

**Table 2** Practical recommendations for screening, monitoring, and management of impulse control disorder in patients treated with dopamine agonists for pituitary disease

Stage	Recommendations
Before DA therapy	<ul style="list-style-type: none"> <li>Assess the indication for DA use</li> <li>Assess the presence of ICD</li> <li>Conduct a thorough assessment of ICD risk factors considering personal and family psychiatric illness</li> <li>Start low-dose DA</li> <li>Educate the patient and accompany family members about the potential risk of ICD</li> <li>Discuss alternative treatment options: OCP, surgery</li> </ul>
During DA therapy	<ul style="list-style-type: none"> <li>Monitor closely for the development of ICD on each visit (involve the patient and other family members)</li> <li>Periodic use of impulsivity questionnaires (every 6–12 mo)<sup>a</sup></li> </ul>
After ICD detection	<ul style="list-style-type: none"> <li>Assess the type of ICD</li> <li>Assess severity and impact on QoL</li> <li>Reduce the dose of DA</li> <li>Involve psychiatrist</li> <li>If there is no improvement, discuss in MDT and consider an alternative approach (one or more):                             <ul style="list-style-type: none"> <li>Discontinue DA therapy</li> <li>Surgery</li> <li>Radiotherapy</li> <li>Cognitive behavioral therapy or medical treatment for ICD<sup>a</sup></li> </ul> </li> </ul>

Abbreviations: DA, dopamine agonist; ICD, impulse control disorder; MDT, multidisciplinary team; OCP, oral contraceptive pill; QoL, quality of life.

<sup>a</sup>In collaboration with a psychiatrist or psychologist.

**Authors' Contribution**

K.A. conceived the article's concept, coordinated its design, and performed the literature search. M.A. reviewed the data and edited the manuscript. Both authors read and approved the final manuscript.

**Conflict of Interest**

None declared.

**Acknowledgment**

The authors thank Dr. Mohammed Alkuwaiti for reviewing the manuscript and suggesting its enhancement.

**References**

- Al-Dahmani K, Mohammad S, Imran F, et al. Sellar masses: an epidemiological study. *Can J Neurol Sci* 2016;43(02):291–297
- Tritos NA, Miller KK. Diagnosis and management of pituitary adenomas: a review. *JAMA* 2023;329(16):1386–1398
- Aldahmani KM, AlMalki MH, Beshyah SA. A rational approach to the evaluation and management of patients with hyperprolactinemia. *Ibnosina J Med Biomed Sci* 2020;12:90–97
- Borovac JA. Side effects of a dopamine agonist therapy for Parkinson's disease: a mini-review of clinical pharmacology. *Yale J Biol Med* 2016;89(01):37–47

- 5 Weintraub D, Mamikonyan E. Impulse control disorders in Parkinson's disease. *Am J Psychiatry* 2019;176(01):5–11
- 6 Thondam SK, Alusi S, O'Driscoll K, et al. Impulse control disorder in a patient on long-term treatment with bromocriptine for a macroprolactinoma. *Clin Neuropharmacol* 2013;36(05):170–172
- 7 AlMalki MH, Alsuraikh MA, AlMalki E, et al. Impulse control disorders in patients with dopamine agonist-treated pituitary adenomas: a cross-sectional multicenter study. *Pituitary* 2024;27(02):197–203
- 8 Bancos I, Nannenga MR, Bostwick JM, et al. Impulse control disorders in patients with dopamine agonist-treated prolactinomas and nonfunctioning pituitary adenomas: a case-control study. *Clin Endocrinol (Oxf)* 2014;80(06):863–868
- 9 Celik E, Ozkaya HM, Poyraz BC, et al. Impulse control disorders in patients with prolactinoma receiving dopamine agonist therapy: a prospective study with 1 year follow-up. *Endocrine* 2018;62(03):692–700
- 10 Dogansen SC, Cikrikcili U, Oruk G, et al. Dopamine agonist-induced impulse control disorders in patients with prolactinoma: a cross-sectional multicenter study. *J Clin Endocrinol Metab* 2019;104(07):2527–2534
- 11 Hinojosa-Amaya JM, Johnson N, González-Torres C, et al. Depression and impulsivity self-assessment tools to identify dopamine agonist side effects in patients with pituitary adenomas. *Front Endocrinol (Lausanne)* 2020;11:579606
- 12 De Sousa SMC, Baranoff J, Rushworth RL, et al. Impulse control disorders in dopamine agonist-treated hyperprolactinemia: prevalence and risk factors. *J Clin Endocrinol Metab* 2020;105(03):dgz076
- 13 Beccuti G, Guaraldi F, Natta G, et al. Increased prevalence of impulse control disorder symptoms in endocrine diseases treated with dopamine agonists: a cross-sectional study. *J Endocrinol Invest* 2021;44(08):1699–1706
- 14 Sanjan G, Das L, Ahuja CK, et al. Impulse control disorders with short-term use of cabergoline in macroprolactinomas: a prospective study with a brief review of literature. *Neurol India* 2023;71(01):107–112
- 15 Ozkaya HM, Sahin S, Korkmaz OP, et al. Patients with acromegaly might not be at higher risk for dopamine agonist-induced impulse control disorders than those with prolactinomas. *Growth Horm IGF Res* 2020;55:101356
- 16 Martinkova J, Trejbalova L, Sasikova M, et al. Impulse control disorders associated with dopaminergic medication in patients with pituitary adenomas. *Clin Neuropharmacol* 2011;34(05):179–181
- 17 Ke X, Wang L, Chen M, et al. The side effects of dopamine receptor agonist drugs in Chinese prolactinoma patients: a cross sectional study. *BMC Endocr Disord* 2022;22(01):97
- 18 Mohammad MM, Alidrisi HA, Mansour AA. Impulse control disorders in Southern Iraqi patients medicated with cabergoline for prolactinoma. *Cureus* 2024;16(04):e58516
- 19 Ozdeniz Varan E, Gurvit H. Effect of dopaminergic therapy on impulse control disorders in patients with a prolactinoma. *Cogn Behav Neurol* 2023;36(01):1–8
- 20 Hamblin R, Karavitaki N. Impulse control disorders in patients with pituitary tumors treated with dopamine agonists: a systematic review. *Arch Med Res* 2023;54(08):102910
- 21 Petersenn S, Fleseriu M, Casanueva FF, et al. Diagnosis and management of prolactin-secreting pituitary adenomas: a Pituitary Society International Consensus Statement. *Nat Rev Endocrinol* 2023;19(12):722–740
- 22 De Sousa SMC. Dopamine agonist therapy for prolactinomas: do we need to rethink the place of surgery in prolactinoma management? *Endocr Oncol* 2022;2(01):R31–R50
- 23 Barake M, Klibanski A, Tritos NA. MANAGEMENT OF ENDOCRINE DISEASE: impulse control disorders in patients with hyperprolactinemia treated with dopamine agonists: how much should we worry? *Eur J Endocrinol* 2018;179(06):R287–R296
- 24 Falhammar H, Yarker JY. Pathological gambling and hypersexuality in cabergoline-treated prolactinoma. *Med J Aust* 2009;190(02):97
- 25 Moore TJ, Glenmullen J, Mattison DR. Reports of pathological gambling, hypersexuality, and compulsive shopping associated with dopamine receptor agonist drugs. *JAMA Intern Med* 2014;174(12):1930–1933