Cabergoline and Impulse Control Disorders: Screening Patients with Pituitary Adenomas in an Endocrinology Clinic

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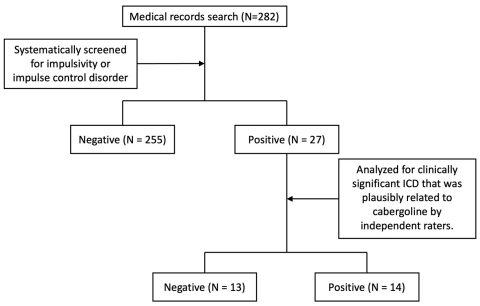
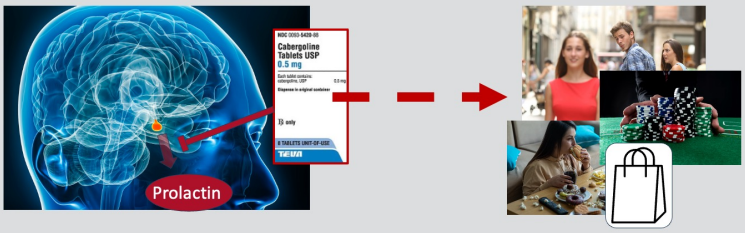
Background

Cabergoline is a dopamine agonist that is a mainstay in the treatment of prolactinoma. The development of de novo impulse control disorders (ICDs) are increasingly recognized as a side effect of dopamine agonist therapy with a prevalence of up to 59.8%[1]. This study investigated risk factors for the development of ICDs and whether current standard-of-care screening practices are effective in detecting this side effect.

Methods

An EMR search was conducted for patients who had seen an endocrinologist for the past 10 years, been diagnosed with pituitary adenoma, and had been prescribed cabergoline. Records were screened systematically for evidence of impulse control disorder. Charts were reviewed for documentation of screening for ICD on first visit, screening for ICD at any time, and information provided of risk of ICD. Charts were reviewed for previously reported risk factors for developing ICD. Positive screens where then reviewed in depth for whether the patient had developed a *clinically significant* ICD that was *plausibly related* to prescription of cabergoline by two independent raters.





Results

	ICD Related to Cabergoline No (N=268)	Yes (N=14)	Total (N=282)	P-value
Age				0.86[1]
N (Missing)	268 (0)	14 (0)	282 (0)	
Mean (SD)	45.3 (16.62)	43.4 (13.85)	45.2 (16.48)	
Median (IQR)	43.0 (32.0, 56.5)	42.0 (34.0, 57.0)	43.0 (32.0, 57.0)	
Range	19.0, 91.0	19.0, 62.0	19.0, 91.0	
Gender, n (%)				**0.001**[2]
Female	159 (59.3%)	2 (14.3%)	161 (57.1%)	
Male	109 (40.7%)	12 (85.7%)	121 (42.9%)	
Ethnicity, n (%)				1.00[2]
Hispanic or Latino	26 (9.7%)	1 (7.1%)	27 (9.6%)	
Not Hispanic or Latino	240 (89.6%)	13 (92.9%)	253 (89.7%)	
Unknown	2 (0.7%)	0 (0.0%)	2 (0.7%)	
Race, n (%)				0.17[2]
Asian	3 (1.1%)	0 (0.0%)	3 (1.1%)	
Black or African American	22 (8.2%)	0 (0.0%)	22 (7.8%)	
Hispanic	1 (0.4%)	1 (7.1%)	2 (0.7%)	
Other	25 (9.3%)	0 (0.0%)	25 (8.9%)	
Unknown	2 (0.7%)	0 (0.0%)	2 (0.7%)	
White or Caucasian	215 (80.2%)	13 (92.9%)	228 (80.9%)	
Smoking status, n (%)				0.77[2]
Current	22 (8.2%)	0 (0.0%)	22 (7.8%)	
Former	64 (23.9%)	3 (21.4%)	67 (23.8%)	
Never	180 (67.2%)	11 (78.6%)	191 (67.7%)	
Never Assessed	2 (0.7%)	0 (0.0%)	2 (0.7%)	
Testosterone therapy in males, n (%)				0.80[3]
No	49 (46.2%)	6 (50.0%)	55 (46.6%)	
Yes	57 (53.8%)	6 (50.0%)	63 (53.4%)	
Missing	3	0	3	
Range	0.3, 14.0	0.5, 6.0	0.3, 14.0	
Psychiatric diagnosis, n (%)				0.37[2]
No	194 (72.4%)	12 (85.7%)	206 (73.0%)	
Yes	74 (27.6%)	2 (14.3%)	76 (27.0%)	
Taking psychiatric medication, n (%)				0.48[2]
No	45 (16.8%)	1 (7.1%)	46 (16.3%)	
Yes	223 (83.2%)	13 (92.9%)	236 (83.7%)	
Screened for ICD on first visit, n (%)				0.31[2]
Informed of Risk	32 (19.9%)	4 (33.3%)	36 (20.8%)	
Not screened or informed	120 (74.5%)	7 (58.3%)	127 (73.4%)	
Screened for ICD	9 (5.6%)	1 (8.3%)	10 (5.8%)	
Screened/informed	41 (25.5%)	5 (41.7%)	46 (26.6%)	
Missing	107	2	109	
Ever screened for ICD, n (%)				**<.0001**[2]
Not screened for ICD	222 (83.1%)	1 (7.1%)	223 (79.4%)	
Screened for ICD	45 (16.9%)	13 (92.9%)	58 (20.6%)	
Missing	1	0	1	
Maximum weekly dose (mg)				**0.01**[1]
N (Missing)	254 (14)	14 (0)	268 (14)	
Mean (SD)	1.3 (1.42)	2.2 (1.83)	1.3 (1.45)	
Median (IQR)	1.0 (0.5, 1.5)	1.5 (1.0, 3.0)	1.0 (0.5, 1.5)	
Range	0.3, 14.0	0.5, 6.0	0.3, 14.0	

[1]Wilcoxon rank sum p-value; [2]Fisher Exact p-value; [3]Chi-Square p-value;

Discussion and Conclusion

Higher doses of cabergoline and male sex were risk factors for the development of ICD, as has been reported previously, while testosterone therapy and smoking status were not in contrast to prior reports[2]. Comorbid psychiatric diagnosis or prescription of psychotropic medications did not increase the risk of ICD which fills an important gap in the literature. Finally, only a fraction of the population was ultimately screened, likely leading to the low prevalence.

Current practice falls short of the standard of care to screen every patient for ICD before starting cabergoline, and this study demonstrates that if not proactively screened it is unlikely that cases of de novo ICDs will be identified. This argues for universal screening with a validated screening tool to improve reliability.

References

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2. Barake, M., Klibanski, A., & Tritos, N. A. (2018). Management of endocrine disease: Impulse control disorders in patients with hyperpolactinemia treated with dopamine agonists: HOW MUCH SHOULD WE WORRY? *European Journal of Endocrinology*, *179*(6). https://doi.org/10.1530/eje-18-0667