

Psychiatric side effects of cabergoline treatment of hyperprolactinaemia: risk factors and prevalence of patient counselling and monitoring

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INTRODUCTION

- Patients receiving dopamine agonists for hyperprolactinaemia are at increased risk of psychiatric side effects¹. These include mood disturbances, personality changes and impulse control disorders².
- Proposed risk factors for developing impulse control disorders include: a history of psychiatric disorder, younger age, male sex, being single, current smoking and alcohol use^{2,3}.

AIMS

- In patients receiving cabergoline for hyperprolactinaemia, we aimed to:
1. Identify the incidence and potential risk factors for the the development of psychiatric side effects.
 2. Review the frequency of patient counselling and monitoring regarding these side effects at treatment initiation and follow-up.

METHODS

- A single-centre retrospective cohort study of hyperprolactinaemia patients (n=257, 61 males, 196 females) who received an outpatient cabergoline prescription between January 2018 and December 2022.
- Data collection included cabergoline dose and duration, sex hormones and prolactin, psychiatric side effect counselling and monitoring.
- Risk factors for development of psychiatric side effects were assessed using multiple logistic regression analysis.

RESULTS

- 8.6% (n=22) developed psychiatric side effects secondary to cabergoline, with mood changes and anxiety being the most common (68.2%, n=15).
- Mean time between cabergoline initiation and psychiatric side effect onset was 8.5 ± 3.4 months. 40.9% (n=9) of patients reported psychiatric side effects within a month of cabergoline initiation and 77.3% (n=17) within 12 months.
- Baseline hypogonadotrophic hypogonadism increased the risk of developing psychiatric side effects (OR=8.22; CI=1.62 to 150.1; $p=0.04$). However, baseline prolactin, cabergoline duration and cumulative dose did not. A sex specific analysis, confirmed no difference in serum testosterone between men who did and did not develop psychiatric side effects with cabergoline treatment.
- Over the five-year study period, 47.5% of patients (n=122) were counselled about psychiatric side effects prior to cabergoline initiation (Figure 1A), and there was enquiry into these at least once during follow-up in 48.6% of patients (n=125) (Figure 1B).
- The prevalence of both counselling and monitoring for psychiatric side effects increased year-on-year from 2018 to 2021 (Figure 1A & B).

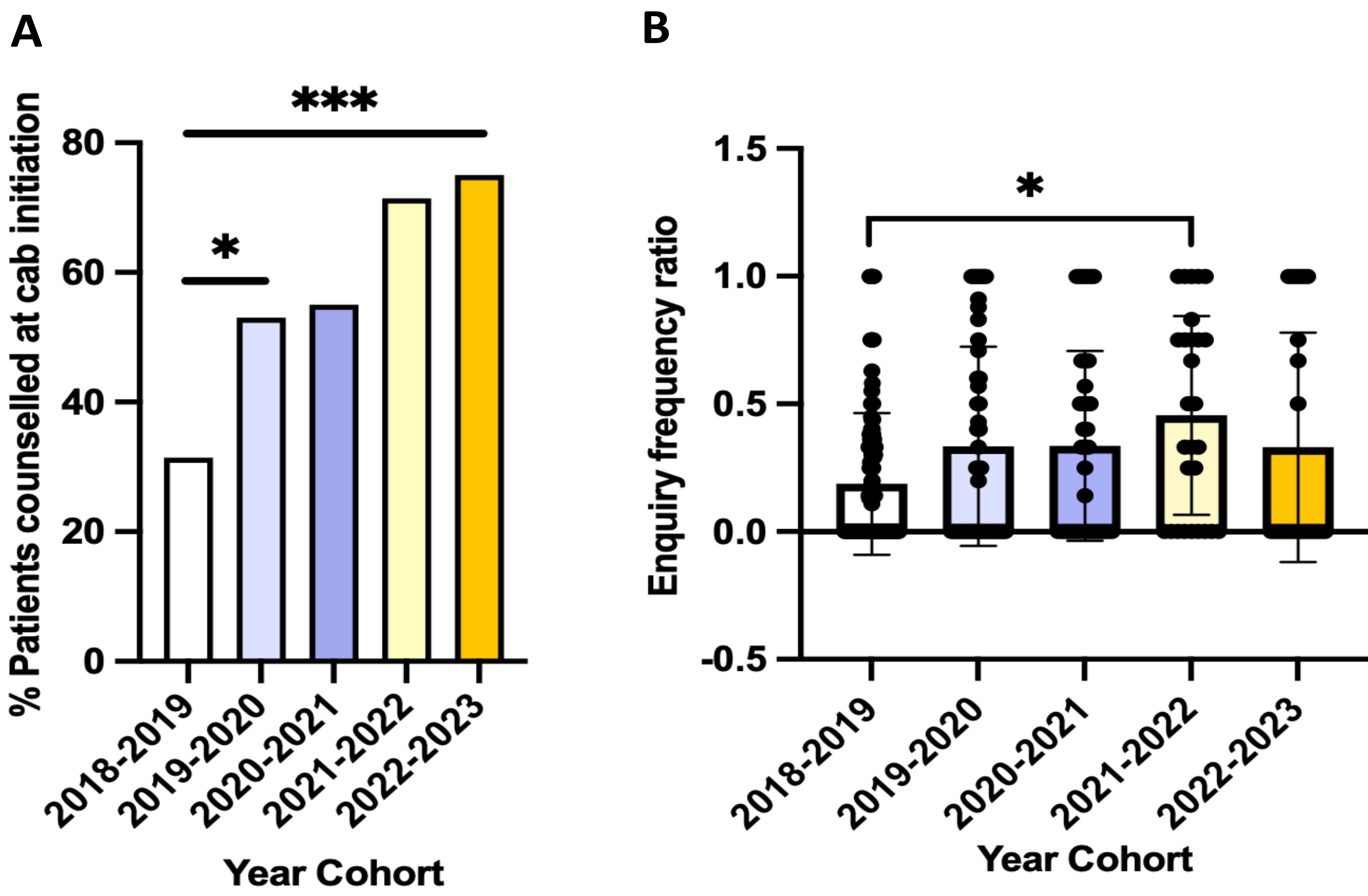


Figure 1: Year-on-year changes in:
A) Proportion of patients counselled at cabergoline initiation between January 2018 and December 2022. $p < 0.05$ was considered statistically significant. * indicates $p < 0.05$, *** indicates $p < 0.001$.
B) Enquiry frequency ratios between January 2018 and February 2023. Comparison of the number of enquiries made to the number of follow-up appointments attended. $p < 0.05$ was considered statistically significant. * indicates $p < 0.05$.

CONCLUSIONS

- In this retrospective cohort study, a psychiatric side effect incidence of 8.6% was identified. This is low in comparison to previous studies which report incidence of impulse control disorders ranging from 8%³ to 60%⁴. Mood changes and anxiety were the most frequently reported psychiatric side effect in this cohort, whereas impulse control disorders were more prevalent in the literature^{1,2}.
- These findings support the need for healthcare professionals to provide counselling regarding psychiatric side effects prior to cabergoline initiation in all patients, particularly in those with baseline hypogonadotrophic hypogonadism.
- For optimal patient safety, a more consistent approach to counselling and monitoring is needed. A potential solution is a standardised questionnaire, and this warrants further exploration.

REFERENCES

1. Ioachimescu AG, Flesteriu M, Hoffman AR, Vaughan III TB, Katznelson L. Psychological effects of dopamine agonist treatment in patients with hyperprolactinemia and prolactin-secreting adenomas. *European journal of endocrinology*. 2019;180(1): 31-40. <https://doi.org/10.1530/EJE-18-0682>.
2. Dogansen SC, Cikrikcili U, Oruk G, Kutbay NO, Tanrikulu S, Hekimsoy Z, et al. Dopamine Agonist-Induced Impulse Control Disorders in Patients With Prolactinoma: A Cross-Sectional Multicenter Study. *The journal of clinical endocrinology and metabolism*. 2019;104(7): 2527-2534. <https://doi.org/10.1210/je.2018-02202>.
3. De Sousa SMC, Baranoff J, Rushworth RL, Butler J, Sorbello J, Vorster J, et al. Impulse Control Disorders in Dopamine Agonist-Treated Hyperprolactinemia: Prevalence and Risk Factors. *The journal of clinical endocrinology and metabolism*. 2019;105(3): e108-e118. <https://doi.org/10.1210/clinem/dgz076>.
4. Celik E, Ozkaya HM, Poyraz BC, Saglam T, Kadioglu P. Impulse control disorders in patients with prolactinoma receiving dopamine agonist therapy: a prospective study with 1 year follow-up. *Endocrine*. 2018;62(3): 692-700. <https://doi.org/10.1007/s12020-018-1744-8>.