

## Double Trouble: Antipsychotics in the Treatment of Antipsychotic-Induced Hyperprolactinemia

**Presentation Date:** May 25<sup>th</sup>, 2022

**Presenter:** Emily Thacker, PharmD

PGY-1 Pharmacy Resident

UPMC Western Psychiatric Hospital

### **Abstract**

Hyperprolactinemia is a common, but troubling adverse effect that can be observed during treatment with antipsychotic medications. Current treatment for antipsychotic-induced hyperprolactinemia is limited, with traditional therapies such as bromocriptine and cabergoline causing psychiatric decompensation and other adverse effects. Multiple pharmacotherapy options including Metformin and other herbal medications have been investigated for the treatment of antipsychotic-induced hyperprolactinemia, but convincing evidence is lacking. Third generation antipsychotics such as aripiprazole have shown promise in this area, but recommendations on their proper use as well as their overall safety and efficacy is controversial.

### **Audience Questions**

1. Which of the following is true regarding the management of antipsychotic induced hyperprolactinemia?
  - a. Prolactin levels should be monitored regularly in all patients taking antipsychotics
  - b. Cabergoline or Bromocriptine can and should be used in any patient with suspected antipsychotic induced HPL
  - c. Prolactin has a clear dose-response relationship and can be lowered by decreasing antipsychotic doses
  - d. Cabergoline and Bromocriptine are poorly tolerated and may increase the incidence of psychiatric decompensation
2. In treating hyperprolactinemia, aripiprazole functions as a \_\_\_\_\_ which \_\_\_\_\_ dopamine levels in the pituitary gland.
  - a. Dopamine agonist, increases
  - b. Dopamine partial agonist, normalizes
  - c. Dopamine antagonist, decreases
  - d. Dopamine partial agonist, doesn't affect
3. Which of the following is true regarding the use of dual antipsychotic therapy?
  - a. Dual antipsychotic therapy has been shown to be safe and efficacious for select patients
  - b. Current guidelines recommend against this strategy
  - c. Current guidelines recommend dual antipsychotic therapy as a first-line treatment for schizophrenia
  - d. Combinations of antipsychotics must include agents from different generations to ensure safety
4. HF is a 25 YOM who has been taking daily Risperidone 4 mg for several months. He reports that his schizophrenia symptoms are well controlled on this regimen. However, he has been experiencing unbearable sexual dysfunction, galactorrhea, and gynecomastia. What could you recommend to treat these symptoms?
  - a. Bromocriptine 5 mg daily
  - b. Decrease risperidone to 2 mg daily
  - c. Initiate aripiprazole 5 mg daily
  - d. Discontinue risperidone, start haloperidol

## References

1. Chen, J. X., et al. (2015). Adjunctive aripiprazole in the treatment of risperidone-induced hyperprolactinemia: A randomized, double-blind, placebo-controlled, dose-response study. *Psychoneuroendocrinology*, *58*, 130–140.
2. Clayton, A. H., Ivkovic, J., Chen, D., George, V., & Hobart, M. (2020). Effect of Brexpiprazole on Prolactin and Sexual Functioning: An Analysis of Short- and Long-Term Study Data in Major Depressive Disorder. *Journal of clinical psychopharmacology*, *40*(6), 560–567.
3. Ioachimescu AG, Fleşeriu M, Hoffman AR, Vaughan TB III, Katznelson L. Psychological effects of dopamine agonist treatment in patients with hyperprolactinemia and prolactin-secreting adenomas. *European Journal of Endocrinology* 2019 180 31–40.
4. Johan Verhelst et al., Cabergoline in the Treatment of Hyperprolactinemia: A Study in 455 Patients, *The Journal of Clinical Endocrinology & Metabolism*, Volume 84, Issue 7, 1 July 1999, Pages 2518–2522
5. Keepers et. al. (Systematic Review) (2020). The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia. *The American journal of psychiatry*, *177*(9), 868–872.
6. Laszlovszky, I., Barabácssy, Á., & Németh, G. (2021). Cariprazine, A Broad-Spectrum Antipsychotic for the Treatment of Schizophrenia: Pharmacology, Efficacy, and Safety. *Advances in therapy*, *38*(7), 3652–3673. <https://doi.org/10.1007/s12325-021-01797-5>
7. Lee, M. S., Song, H. C., An, H., Yang, J., Ko, Y. H., Jung, I. K., & Joe, S. H. (2010). Effect of bromocriptine on antipsychotic drug-induced hyperprolactinemia: eight-week randomized, single-blind, placebo-controlled, multicenter study. *Psychiatry and clinical neurosciences*, *64*(1), 19–27. <https://doi.org/10.1111/j.1440-1819.2009.02032.x>
8. Lee, BH, Han, CS, Kim, KH (2005) Treatment in risperidone-induced amenorrhoea. *International Journal of Psychiatry in Clinical Practice*, *9*: 29–34.
9. Lehman, A. F et. al., American Psychiatric Association, & Steering Committee on Practice Guidelines (2004). Practice guideline for the treatment of patients with schizophrenia, 2<sup>nd</sup> edition. *The American journal of psychiatry*, *161*(2 Suppl), 1–56.
10. Li, X., Tang, Y., & Wang, C. (2013). Adjunctive aripiprazole versus placebo for antipsychotic-induced hyperprolactinemia: meta-analysis of randomized controlled trials. *PLoS one*, *8*(8), e70179.
11. Majumdar, A., & Mangal, N. S. (2013). Hyperprolactinemia. *Journal of human reproductive sciences*, *6*(3), 168–175.
12. Melmed, S., Casanueva, F. F., Hoffman, A. R., Kleinberg, D. L., Montori, V. M., Schlechte, J. A., Wass, J. A., & Endocrine Society (2011). Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guideline. *The Journal of clinical endocrinology and metabolism*, *96*(2), 273–288.
13. Ortiz-Orendain, J., Castiello-de Obeso, S., Colunga-Lozano, L. E., Hu, Y., Maayan, N., & Adams, C. E. (2017). Antipsychotic combinations for schizophrenia. *The Cochrane database of systematic reviews*, *6*(6), CD009005.
14. Potkin, S. G., et al.. (2003). Aripiprazole, an antipsychotic with a novel mechanism of action, and risperidone vs placebo in patients with schizophrenia and schizoaffective disorder. *Archives of general psychiatry*, *60*(7), 681–690.
15. Soto-Albors, C. E., Randolph, J. F., Ying, Y. K., & Riddick, D. H. (1987). Medical management of hyperprolactinemia: a lower dose of bromocriptine may be effective. *Fertility and sterility*, *48*(2), 213–217.
16. Stahl, & Grady, M. M. (2004). A Critical Review of Atypical Antipsychotic Utilization: Comparing Monotherapy with Polypharmacy and Augmentation. *Current Medicinal Chemistry*, *11*(3), 313–327.
17. Tewksbury, A., & Olander, A. (2016). Management of antipsychotic-induced hyperprolactinemia. *The mental health clinician*, *6*(4), 185–190.
18. Wahl, R., & Ostroff, R. (2005). Reversal of symptomatic hyperprolactinemia by aripiprazole. *The American journal of psychiatry*, *162*(8), 1542–1543. <https://doi.org/10.1176/appi.ajp.162.8.1542-a>
19. Xu LP, Ji JY, Shi H, Zhai FL, Zhang B, et al... (2006) A control study of aripiprazole in the treatment of hyperprolactinemia by antipsychotics *Chin J of Behavioral Med Sci*: 718–720.
20. Yasui-Furukori, N. et al. (2010). Dose-Dependent Effects of Adjunctive Treatment With Aripiprazole on Hyperprolactinemia Induced by Risperidone in Female Patients With Schizophrenia. *Journal of Clinical Psychopharmacology*, *30* (5), 596-599.
21. Zhang, L., Qi, H., Xie, Y. Y., Zheng, W., Liu, X. H., Cai, D. B., Ng, C. H., Ungvari, G. S., & Xiang, Y. T. (2021). Efficacy and Safety of Adjunctive Aripiprazole, Metformin, and Paeoniae-Glycyrrhiza Decoction for Antipsychotic-Induced Hyperprolactinemia: A Network Meta-Analysis of Randomized Controlled Trials. *Frontiers in psychiatry*, *12*, 728204. <https://doi.org/10.3389/fpsy.2021.728204>
22. Zheng, W., Cai, D. B., Yang, X. H., Ungvari, G. S., Ng, C. H., Shi, Z. M., Hu, M. L., Ning, Y. P., & Xiang, Y. T. (2019). Adjunctive aripiprazole for antipsychotic-related hyperprolactinemia in patients with first-episode schizophrenia: a meta-analysis. *General psychiatry*, *32*(5), e100091. <https://doi.org/10.1136/gpsych-2019-100091>