

Department of Analyzing Benefit vs Harm in Managing Clinically Significant Hyperprolactinemia in Patient with Treatment Resistant Schizophrenia

Sarah E. Bignault MS3; Mohamed T. Jasser DO; Candace Perry MD



INTRODUCTION:

Prolactin is a hormone released from the anterior pituitary that is involved in the functioning of the reproductive, endocrine, and metabolic systems. It is synthesized and secreted by lactotrophs in response to steroids, peptides, and neurotransmitters. Inhibitory regulation is managed by dopamine binding to D2 receptors on the membranes of these cells. Antipsychotic medications remove this regulation by blocking D2 receptors, leading to potential hyperprolactinemia through uncontrolled secretion (2). Hyperprolactinemia can be asymptomatic but can also have long term consequences including amenorrhea, galactorrhea, gynecomastia, infertility, and osteoporosis (3). According to literature, if a patient has symptomatic hyperprolactinemia, the medication should be reduced in dose and serum prolactin should be remeasured after three days (6). If this is unsuccessful, a dopamine agonist such as bromocriptine can be added, or the medication should be switched to a prolactin sparing drug, such as aripiprazole or clozapine (5).

The case presented is used to highlight the importance of an integrative approach to care when it comes to psychiatric patients dealing with complicated medical comorbidities. It was only through a collaborative effort was a proper analysis of the risks and benefits of each possible treatment properly weighed and a decision made with the patient that allowed her to achieve a positive outcome.

CASE PRESENTATION:

This report describes the case of a 40-year-old female with past psychiatric history of schizophrenia. The patient has a history of extensive inpatient psychiatric hospitalizations, the shortest duration of which was several months. She was admitted for this most recent hospitalization in June 2020. She suffers from severe command hallucinations, which prompted a previous suicide attempt by overdose, as well as chronic derogatory auditory hallucinations which cause her to believe she is responsible for plagues, burning, and destruction. Her numerous episodes of aggression have resulted in attacks on and injury to staff members, requiring her restraint. After multiple failed trials of atypical agents including clozapine and numerous typical agents in both mono-therapy and combination therapy, long acting paliperidone successfully treated her psychosis besides occasional breakthrough symptoms near her next scheduled injection.

In October 2020, while hospitalized, she developed amenorrhea. Labs were taken on October 31st and revealed a markedly elevated prolactin level of 91.5. Serial prolactin levels results were 140.3 on December 11th and 143.9 on January 12th. On January 15th labs showed a prolactin level of 154.0, IGF binding protein 1 of 2.2, TSH of 1.11, Free T4 of 1.26, and AM Cortisol of 9.79. MRI demonstrated a hypo-enhancing mass centered along the posterior aspect of the pituitary gland measuring 15x8x8mm with mild rightward deviation of the pituitary stalk. There was no cavernous sinus inversion or mass effect upon the optic chiasm. This study revealed pituitary macroadenoma with stalk deviation as another potential cause of the patient's hyperprolactinemia.



DISCUSSION:

Although guidelines suggest reducing the dose of the antipsychotic for this patient to manage the potential side effects of hyperprolactinemia, concern for the reemergence of psychosis prompted the search for other alternatives. Previous trials of aripiprazole and clozapine, the suggested alternatives, were unable to control her symptoms. Adding a dopamine agonist such as bromocriptine was not an optimal choice for this case. Because lowering her dose of paliperidone could potentially cause harm to the patient, in accordance with the ethical principal of Do No Harm, we refrained from reducing the dose and chose to pursue interval monitoring, as well as other potential causes of her hyperprolactinemia.

This case highlights the analysis of risks versus benefits and the treatment approach that needs to be considered when approaching medication management when the potentially detrimental long-term effects to a patient due to treatment can be significant/ when psychosis is severe and refractory to most medication regimens, it is important to consider the potential harm in decreasing the dose, switching the drug, or adding a dopamine agonist compared to the symptoms from hyperprolactinemia. Additionally, it is important to recognize that medications may not be the sole cause of hyperprolactinemia and evaluation for other etiologies may be necessary for selected patients.

CONCLUSION:

The patient presented suffered from psychotic episodes which were unable to be adequately controlled with most antipsychotic regimens. Long acting paliperidone was able to control her symptoms, but she developed hyperprolactinemia, a known side effect. Despite this, we chose not to reduce her antipsychotic dose because controlling the severity of her psychosis was deemed more beneficial to the patient than the side effects of hyperprolactinemia. Additionally, because hyperprolactinemia has other potential etiologies besides antipsychotic usage, we suggest it is important for the well-being of the patient to thoroughly investigate those alternatives before making decisions that could impact the patient's quality of life. Therefore, instead of simply following protocol, we argue that in accordance with the ethical principle of Do No Harm, patients should be evaluated on a case-by-case basis by multidisciplinary teams to balance the benefits and adverse effects of medications on their quality of life.

REFERENCES:

- Ajmal A, Joffe H, Nachtigall LB. Psychotropic-induced hyperprolactinemia: a clinical review. Psychosomatics. 2014 Jan-Feb;55(1):29-36. doi: 10.1016/j.psym.2013.08.008. Epub 2013 Oct 18. PMID: 24140188.
- 2. Besnard I, Auclair V, Callery G, Gabriel-Bordenave C, Roberge C. Hyperprolactinémies induites par les antipsychotiques : physiopathologie, clinique et surveillance [Antipsychotic-drug-induced hyperprolactinemia: physiopathology, clinical features and guidance]. Encephale. 2014 Feb;40(1):86-94. French. doi: 10.1016/j.encep.2012.03.002. Epub 2013 Aug 5. PMID: 23928066.
- 3. Bostwick JR, Guthrie SK, Ellingrod VL. Antipsychotic-induced hyperprolactinemia. Pharmacotherapy. 2009 Jan;29(1):64-73. doi: 10.1592/phco.29.1.64. PMID: 19113797.
- 4. Majumdar A, Mangal NS. Hyperprolactinemia. J Hum Reprod Sci. 2013 Jul;6(3):168-75. doi: 10.4103/0974-1208.121400. PMID: 24347930; PMCID: PMC3853872.
- 5. Raveendranthan D, Rao NP, Rao MG, Mangot AG, Varambally S, Kesavan M, Venkatasubramanian G, Gangadhar BN. Add-on Aripiprazole for Atypical Antipsychotic-induced, Clinically Significant Hyperprolactinemia. Indian J Psychol Med. 2018 Jan-Feb;40(1):38-40. doi: 10.4103/IJPSYM_147_17. PMID: 29403128; PMCID: PMC5795677.
- 6. Shlomo Melmed, Felipe F. Casanueva, Andrew R. Hoffman, David L. Kleinberg, Victor M. Montori, Janet A. Schlechte, John A. H. Wass, Diagnosis and Treatment of Hyperprolactinemia: An Endocrine Society Clinical Practice Guideline, *The Journal of Clinical Endocrinology & Metabolism*, Volume 96, Issue 2, 1 February 2011, Pages 273–288, https://doi.org/10.1210/jc.2010-1692
- 7. Tewksbury A, Olander A. Management of antipsychotic-induced hyperprolactinemia. Ment Health Clin [Internet]. 2016;6(4):185-90. DOI: 10.9740/mhc.2016.07.185.
- 8. Wu H, Deng L, Zhao J, Li L, Chen J. Osteoporosis associated with antipsychotic treatment in schizophrenia. Int J Endocrinol. 2013;2013:167138. doi: 10.1155/2013/167138. Epub 2013 Apr 17. PMID: 23690768; PMCID: PMC3652172.