CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
http://doi.org/10.5281/zenodo.4078280

Available online at: http://www.iajps.com *A Case Report*

A CASE REPORT ON LEVOSULPIRIDE INDUCED HYPERPROLACTINEMIA

[1]Dr. Reeja KR, [1]Dr. Ponnu Sara Joseph, [1]Dr. Grace Mary John, [1]Dr. Soorya Soman, [2]Dr. George M Chandy

[1]Clinical Specialist, Department of Clinical Pharmacy, Believers church Medical College Hospital, Thiruvalla, Kerala

[2]Director and Head of the Department of Gastroenterology and Hepatology, Believers church Medical College Hospital, Thiruvalla, Kerala

Article Received: September 2020 **Accepted:** September 2020 **Published:** October 2020

Abstract:

What is known and objectives: *Hyperprolactinemia is a condition of increased serum prolactin level. The main physiologic control of prolactin secretion is exerted by the inhibition of dopamine, which is considered to be the cause of drug induced hyperprolactinemia.*

Case Summary: *We describe a case report of a patient who presented with galactorrhoea secondary to Levosulpiride intake for treating functional dyspepsia.*

What is new and Conclusion: *The incidence of pharmacologic hyperprolactinemia is underestimated. A detailed Medication Reconciliation done by clinical pharmacist can help in identifying such rare ADRs, which aids in treating the patient efficiently and cost effectively.*

Corresponding author:

Dr. George M Chandy

Director and Head of the Department of Gastroenterology and Hepatology,
Believers church Medical College Hospital,
Thiruvalla, Kerala

QR code

Please cite this article in press Ponnu Sara Joseph et al, ***A Case Report On Levosulpiride Induced hyperprolactinemia.,*** *Indo Am. J. P. Sci, 2020; 07(10).*

1| DETAILS OF THE CASE:

A 50-year-old lady presented to our Gynaecology department with complaints of galactorrhea for a week. She was known to have hypertension and was on Cilnidipine for 6 months

She had recently consulted a Gastroenterologist for her symptoms of dyspepsia. After detailed evaluation including a Gastroscopy, a diagnosis of Functional dyspepsia was made. For this, she was prescribed a combination of sustained release formulation of Esomeprazole 20mg and Levosulpiride 75mg, once daily. She had taken these medications for 2 weeks prior to presentation. She had no symptoms of visual disturbances or headache. There was no similar history in the past. On general examination, her vitals were stable.

A hormonal assay was done, which revealed an elevated serum prolactin level of **272 ng/ml** (normal level for a non-pregnant woman is 2 to 29 ng/ml). While evaluating the causes of galactorrhoea, the medication history was uppermost in the mind of the Clinical Pharmacist, since the patient was taking Levosulpiride. The patient was advised to stay off Levosulpiride therapy. Upon discontinuation, she was found to be symptomatically better and her prolactin level returned to normal of in 2 weeks' time.

2| WHAT IS KNOWN AND OBJECTIVES:

Hyperprolactinemia clinically presents as galactorrhoea and amenorrhea in women and decreased libido and erectile dysfunction in men[1]. Pituitary tumours and breast cancer are malicious etiologies associated with hyperprolactinemia.

The dominant dopaminergic pathway that regulates prolactin secretion is the tuberoinfundibular dopaminergic (TIDA) pathway. Dopamine acts on D2 dopaminergic receptors that are expressed on the cell membrane of the lactotrophs. There is a reduction of prolactin synthesis and secretion by the activation of these D2 receptors[2].

Prevalence of pharmacologic hyperprolactinemia is underestimated. Various drugs identified to cause Hyperprolactinemia are listed in Table 1[3]. According to Petit et al incidence rates of hyperprolactinaemia based on therapeutic drug classes are highest with neuroleptics (31% followed by neuroleptic-like drugs (28%), antidepressants (26%), H2-receptor antagonists (5%) and 10% with others[4]. Recently, case reports have identified the association of atypical antipsychotics and/or prokinetics in causing hyperprolactinemia. The female/male ratio of patients developing drug induced hyperprolactinemia was found to be 5.9 in a pharmacoepidemiological analysis done by Petit et al[4].

Table 1: Drugs known to cause hyperprolactinemia

Antipsychotics Typical	Haloperidol Chlorpromazine, Thiothixene
Antipsychotics Atypical	Risperidone, Amisulpride
Antidepressants	Amitriptyline, Desipramine Clomipramine Amoxapine, Sertraline, Fluoxetine, Paroxetine
Psychotropics	Buspirone Alprazolam
Prokinetics	Metoclopramide, Domperidone
Antihypertesives	Methyldopa, Reserpine, Verapamil
Opiates	Morphine
H_2 Antagonists	Cimetidine, Ranitidine

Functional dyspepsia is defined as chronic disorder (at least 12 weeks) of abdominal pain or discomfort centered in the upper abdomen for which an organic process cannot be identified according to Rome II Criteria[5]. The annual incidence of dyspepsia is approximately 9–10%, out of which 15% of patients have chronic and often severe symptoms[6].

Prokinetic agents are the mainstay of treatment of patients with functional dyspepsia. 3 main prokinetic agents that are widely used are metoclopramide, domperidone, and levosulpiride. Basically, they are antidopaminergic drugs. The prokinetic effect is mediated through the blockade of enteric (neuronal and muscular) inhibtory D2 receptors and thus stimulating and coordinating gastroduodenal motility. Also these drugs increases basal lower esophageal sphincter pressure, inhibits relaxation of the gastric fundus, enhances antral contractility, and relaxes the pyloric sphincter[7].

Levosulpiride is the levo-enantiomer of sulpiride. It is a benzamide derivative classified as an atypical neuroleptic agent and is also a selective dopamine D_2-receptor antagonist. In low doses, Levosulpiride is used in treating functional dyspepsia and depression and high doses are used to treat schizophrenia[8]. Levosulpiride has additional agonist activity on Type 4 serotonergic ($5HT_4$) receptors, thus enhancing its therapeutic efficacy in functional dyspepsia and diabetic gastroparesis[7,9]. Doses of levosulpiride 25mg thrice daily accelerates gastric and gallbladder empting[9]. Double-blind, RCTs of levosulpiride with other dopamine antagonists such as domperidone or metoclopramide have shown that levosulpiride has a superior effect in reducing the intensity of dyspeptic symptoms and in the time necessary to achieve this effect. Inhibition of Prolactin release by blocking the dopaminergic receptors on the pituitary lactotrophs is considered to be the mechanism by which levosulpiride induces hyperprolactinemia[1]. Available literature suggests that Levosulpiride has a 11- 13% incidence of adverse effects[9]. In a study by Lozano et al., galactorrhoea was reported in 26.7% of patients on levosulpiride[10].

Our patient presented with complaints of galactorrhea with no underlying identifiable cause. Before going for a radiological assessment with an MRI to rule out pituitary abnormalities, a Clinical Pharmacist's consultation was sought. Causality assessment for classifying Adverse Drug reaction using Naranjo Probability Scale was found to be 8 (probable ADR). Hence the drug was discontinued based on the probable incidence of this adverse event. The patient recovered after stopping the drug and the prolactin level returned to normal within 2 weeks. Re-challenge was not carried out due to the potential risk involved. Withdrawal of the offending drug alone is sufficient to normalize the raised serum prolactin levels to baseline. Drug induced hyperprolactinemia is reversible and prolactin levels returns to normal in 2 -3 weeks after the discontinuation of the offending drug.

Medication errors are common and usually occur when patients move between healthcare settings and specialties.[11] In our case, the patient was prescribed Levosulpiride by the gastroenterologist for treating functional dyspepsia, whereas the patient consulted the gynaecologist upon occurrence of the adverse drug event secondary to use of this drug. The purpose of Medication reconciliation (MedRec) is to prevent specific Drug Related Problems during transition of care. Inadequate medication history often leads to inappropriate management of the patient. A clear MedRec performed by a clinical pharmacist is an important element of patient safety and this can help in avoiding unnecessary healthcare costs spent for further evaluation.

3| WHAT IS NEW AND CONCLUSION:

To conclude, in any patient who presents with acute onset galactorrhoea, the clinician should assess the patient for a history of using antipsychotic medication, although such drugs may not be used as an antipsychotic. In this case, the patient was not prescribed with levosulpiride as an antipsychotic but for dyspepsia symptoms.

Management options include discontinuation of the suspected drug. Symptoms usually subsides within 2 - 3 weeks. For patients with no relevant drug history and who has persistent symptoms, it is important to exclude other causes of prolactin elevation such as tumors in the hypothalamic-pituitary area, pregnancy, hypothyroidism and chronic renal insufficiency.

A detailed MedRec performed by a clinical pharmacist plays a vital role in identifying Drug Related Problems, and thus, it is an important element of patient safety. Awareness about Levosulpiride and its effect on serum prolactin levels and a careful drug history will help the clinician to make correct diagnosis and avoid unnecessary brain imaging. Clinicians need to be vigilant and informed about this adverse effect and may choose other treatment options, which do not cause dopaminergic blockade.

REFERENCES:

1. Triebel J, Robles-Osorio ML, Garcia-Franco R, Martinez de la Escalera G, Clapp C, Bertsch T. From Bench to Bedside: Translating the Prolactin/Vasoinhibin Axis. Front Endocrinol (Lausanne). 2017;8:342.
2. Kuchay MS, Mithal A. Levosulpiride and Serum Prolactin Levels. Indian J Endocrinol Metab. 2017;21(2):355-8.
3. Torre DL, Falorni A. Pharmacological causes of hyperprolactinemia. Ther Clin Risk Manag. 2007;3(5):929-51.
4. Petit A, Piednoir D, Germain ML, Trenque T. [Drug-induced hyperprolactinemia: a case-non-case study from the national pharmacovigilance database]. Therapie. 2003;58(2):159-63.
5. Drossman DA, Corazziari E, Talley NJ, Thompson WG, Whitehead WE, Rome II. Diagnosis, pathophysiology and treatment: A multinational consensus. Degnon Associates. 2000.
6. Kumar A, Pate J, Sawant P. Epidemiology of functional dyspepsia. J Assoc Physicians India. 2012;60 Suppl:9-12.
7. Corazza GR, Biagi F, Albano O, Bianchi Porro G, Cheli R, Mazzacca G, et al. Levosulpiride in functional dyspepsia: a multicentric, double-blind, controlled trial. Ital J Gastroenterol. 1996;28(6):317-23.
8. Andrade C. Low-dose amisulpride and elevation in serum prolactin. J Clin Psychiatry. 2013;74(6):e558-60.
9. Serra J. [Levosulpiride in the management of functional dyspepsia and delayed gastric emptying]. Gastroenterol Hepatol. 2010;33(8):586-90.
10. Lozano R, Concha MP, Montealegre A, de Leon L, Villalba JO, Esteban HL, et al. Effectiveness and safety of levosulpiride in the treatment of dysmotility-like functional dyspepsia. Ther Clin Risk Manag. 2007;3(1):149-55.
11. Allard J, Carthey J, Cope J, Pitt M, Woodward S. Medication errors: causes, prevention and reduction. Br J Haematol. 2002;116(2):255-65.
12. Pathania M, Malik P, Amisha, Sharma S. Good clinical history scores over extensive workup in unmasking a case of galactorrhoea. BMJ Case Rep. 2018;2018.