

Beyond Pain Relief: A Rare Hormonal Impact of Pregabalin in Fibromyalgia

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ABSTRACT:

Pregabalin (PBG), a widely used anticonvulsant and anxiolytic medication, is known for its efficacy in treating neuropathic pain, generalized anxiety disorder and as an adjunct therapy for partial seizures. Here we present a case of Pregabalin induced hyperprolactinemia in a 18 year old female patient diagnosed with Galactorrhea. Pregabalin inhibits the release of neurotransmitter like Dopamine which is the most important hypothalamic-inhibiting factor of Prolactin (PRL). Dopamine restrains prolactin production, so the more dopamine there is, the less prolactin is released. Prolactin itself enhances the secretion of dopamine, so this creates a negative feedback loop. The rarity of Pregabalin induced hyperprolactinemia warrants attention, as unrecognized and untreated hyperprolactinemia can result in significant morbidity.

KEYWORDS: Pregabalin, Hyperprolactinemia, Fibromyalgia, Neuropathic pain

INTRODUCTION:

Fibromyalgia is a chronic condition marked by persistent and widespread musculoskeletal pain, frequently accompanied by additional symptoms including fatigue, gastrointestinal issues, sleep disturbances and mood alterations. Fibromyalgia appears to represent one end of a spectrum of chronic widespread pain, a condition that may affect 10% to 15% of the general population.¹ For the management of Fibromyalgia, Pregabalin is the first FDA approved drug that can reduce both pain and improve the quality of life and health status among Fibromyalgia patients. Pregabalin (PBG) is a well established central nervous system depressant and a structural analogue of gamma-aminobutyric acid (GABA). As a non-opioid drug, it functions as a $\alpha 2 - \delta$ ligand that modulates the activity of voltage-gated calcium channels. It was initially discovered for treating neuropathic pain associated with diabetic peripheral neuropathy and post herpetic neuralgia (PHN). In June 2005, FDA approved the drug for the treatment of partial onset seizures, with or without secondary generalization in adults, as an adjunctive therapy. Currently, FDA is considering approving Pregabalin as an adjunctive therapy for adults with generalized anxiety disorder (GAD), social anxiety disorder (SAD) and spinal cord injuries.² In the European Union, Pregabalin is indicated for peripheral and central neuropathic pain, epilepsy, and GAD.³ The most frequent undesirable effects noted are dizziness, somnolence, dry mouth, edema, blurred vision, weight gain, endocrine disorders such as thyroid disorder, adrenal insufficiency, and rarely hyperprolactinemia.

CASE REPORT:

This case report highlights an instance of Pregabalin induced hyperprolactinemia in an 18 year old female patient who was prescribed Pregabalin for fibromyalgia. Following the initiation of Pregabalin therapy (75 mg) in 2023 after 2 months the patient presented with Galactorrhoea from the left breast. Pregnancy test was performed and the result found to be negative. Further laboratory tests revealed significantly elevated serum prolactin levels ($>4255.00 \mu\text{IU/mL}$). Later on MRI was performed to test for pituitary gland tumors like prolactinomas, which could present the same. Patient is also not a known case of hypothyroidism, CKD, and has not undergone any breast or spine surgeries. Patient history also revealed that she was not on oral contraceptives or any other supplements. Hence Pregabalin induced hyperprolactinemia was suspected, and the drug was promptly discontinued. Upon discontinuation of Pregabalin, the patient's prolactin levels gradually returned to normal, and the symptoms resolved completely. This case underscores the importance of monitoring for endocrine side effects especially in patients receiving Pregabalin, especially in those presenting with unexplained galactorrhoea.

DISCUSSION:

Pregabalin, a medication structurally similar to gamma-aminobutyric acid (GABA), is used to treat a range of chronic conditions, including chronic pain, partial seizures, sleep and anxiety disorders and fibromyalgia. As a calcium channel antagonist, it reduces the release of neurotransmitters like substance P, norepinephrine, and glutamate, providing pain relief and anxiety reduction.⁽⁴⁾⁽⁵⁾ Hyperprolactinemia (HPL) is a frequently encountered pituitary gland disorder that can arise from diverse causes. Hyperprolactinemia can be caused by medication like sedatives, antidepressants, antipsychotics, opioids, and antihypertensives.⁽⁶⁾ Other less obvious causes could be pregnancy, supplements and contraceptives.

Dopamine, the most important hypothalamic inhibitor of Prolactin (PRL), binds to D2 receptors on lactotroph cells in the anterior pituitary gland. This binding suppresses PRL gene expression and release inhibiting adenylyl cyclase, inositol phosphate metabolism and altering potassium and calcium channels. Several peptide and neurotransmitters like serotonin, estrogens, tachykinins, gonadotropin-releasing hormone associated peptide (GAP), opioids, histamine and GABA also modulate PRL secretion.⁽⁷⁾ GABA primarily secreted in the hypothalamus, has an inhibitory effect. It modulates pituitary hormone secretion through dopaminergic activity or direct influence on anterior pituitary cells. Activation of GABA-A and GABA-B receptors reduces PRL secretion. Pregabalin is similar to GABA but does not affect GABA receptors. It works by blocking calcium channels.

Pregabalin has antiallodynic properties; It works by decreasing the number of pain signals sent out by damaged nerves.⁽⁸⁾ In this case, patient has developed hyperprolactinemia after 2 months of starting therapy with Pregabalin, hence confirming temporal association. Though the exact mechanism isn't clear, its use is likely the cause as other indications have been ruled out systematically. However rechallenge could not be performed owing to patient's mental status.⁽⁹⁾ Hence, concluding that hyperprolactinemia has been caused by Pregabalin use.

According to UMC, 154608 ADR's have been reported by Pregabalin and its analogues, of which 502 involves endocrine disorders, which were earlier deemed to be uncommon.⁽¹⁰⁾ Hyperprolactinemia induced by Pregabalin is still rare, with just 1 case reported in Vigibase. For rigorous evaluation of causality and attributes, we relied on established scales and criteria to perform a comprehensive and standardized evaluation of causality and other attributes. Upon evaluation, the causality was determined to be

“Probable” using the WHO-UMC assessment scale. The type of ADR was classified as “Type C” according to the Rawlins-Thompson classification and severity was assessed as “Level 3, Moderate” based on the modified Hartwig’s scale. As per the WHO criteria, the seriousness of the reaction was categorized as “other medically important” and the outcome of the reaction was “recovering”. According to the Schumock and Thornton scale, the ADR was also deemed as “not preventable”.

In conclusion, Pregabalin-induced hyperprolactinemia presents a significant challenge for patients on therapy. This case study elucidates how a young, female patient with fibromyalgia experienced significant distress due to Pregabalin-induced hyperprolactinemia, emphasizing the urgent need to identify and treat this side effect promptly. Our report is to alert healthcare professionals regarding an uncommon, but harrowing side effect to a commonly used drug like Pregabalin.

DECLARATION OF PATIENT CONSENT:

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity.

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