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Case Study

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LEVOSULPIRIDE INDUCED GALACTORRHEA: A CASE REPORT

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ABSTRACT

Drug induced galactorrhea is a condition of increased prolactin level in the serum caused due to adverse effect of a drug resulting in galactorrhea and irregular menstrual cycle in women. Levosulpiride is a novel drug with antipsychotic, anti-depressant, anti-emetic and anti-dyspeptic actions. Galactorrhea is the secretion of milky discharge from breast in men or women who are not breastfeeding for one year. It may result from excessive secretion of prolactin or increased sensitivity of breast tissue to prolactin. A rare case on levosulpiride induced elevated serum prolactin level presenting as a distressing adverse effect of galactorrhoea in a female patient was reported. It is important to keep a watch on prolactin levels during treatment with levosulpiride. For patients who present as a confirmed case of hyperprolactinemia, it is important to exclude other causes of prolactin elevation. Reporting the case would be a learning point for the fellow health care professionals in optimizing the therapy and requirement of strict monitoring of prescription that would minimize the medication errors.

KEYWORDS: Levosulpiride, galactorrhoea, hyperprolactinemia, prokinetic.

INTRODUCTION

Levosulpiride is the levorotatory enantiomer of sulpiride, a substituted benzamide used for different dyspeptic symptoms due to varied etiologies. It is a novel drug with antipsychotic, antidepressant, antiemetic and anti-dyspeptic actions. The prokinetic effect of levosulpiride is mediated through the blockade of enteric inhibitory dopaminergic type 2 (D2) receptors. The antagonism of central D2 receptors leads to both therapeutic (e.g. antiemetic effect due to D2 receptor blockade in the chemoreceptor trigger zone) and adverse (including hyperprolactinemia) effects.[1] Dopamine is the main endogenous inhibitor of prolactin synthesis and secretion in the anterior pituitary. Levosulpiride causes significant elevation of serum prolactin levels in significant number of patients. The resultant hyperprolactinemia often manifests as distressing menstrual abnormalities and galactorrhoea in females. A significant number of patients who use levosulpiride develop serum prolactin levels of > 200 ng/mL that goes against the classical textbook teaching where pituitary tumour is supposed to be the mostly likely cause. Prolactin is a peptide hormone released from anterior pituitary which in turn is regulated predominantly by inhibitory effect of dopamine and to a small extent by the stimulatory effect of thyrotropin releasing hormone, oxytocin, vasopressin, vasoactive intestinal peptide and angiotensin-II.[2] Any condition that produces imbalance in these substances can lead to elevation of prolactin and cause galactorrhea and menstrual abnormalities.[3] Drugs like antipsychotics, antidepressants, estrogen containing drugs, prokinetics, antihypertensives and opioids that act by blocking D2 receptors or decrease synthesis of dopamine can reduce the hypothalamic inhibitory tone on pituitary and thereby can increase in prolactin secretion which may cause galactorrhea.[4] Careful drug history in patients presenting with high serum prolactin levels will be of great help in reaching the exact diagnosis and avoiding unnecessary brain imaging.

CASE REPORT

A 36 year old lady presented to our hospital outdoor patient department in October 2020 with complaints of abdominal fullness post meals, abdominal bloating, colicky abdominal pain post meals, early satiety and constipation. She was earlier operated thrice. She had a history of caesarean section twice and donor nephrectomy. She had been prescribed with pantoprazole (40 mg) and levosulpiride (75 mg) combination pill once a day for her symptoms. She was relieved of her dyspeptic symptoms and was doing well, but after 2 months of taking these drugs, she developed menstrual irregularity and galactorrhoea. For these symptoms she consulted a gynaecologist at a private clinic and was advised to check serum prolactin levels. Her serum prolactin levels were elevated >200 ng/ml. She was then advised MRI of the pituitary gland by the gynaecologist which turned out to be unremarkable. Cabergoline was

prescribed (0.5 mg twice a week) and then gradually increased to 2 mg per week by the gynaecologist but the symptoms didn't improve. She then consulted us for the unabatable symptoms of galactorrhoea. A review of drug history revealed the intake of levosulpiride. Levosulpiride induced hyperprolactinemia was suspected and hence it was stopped. Results appeared only after a week of stopping levosulpiride. Her serum prolactin level was found to be reduced to 36 ng/ml whereas galactorrhea subsided completely. These findings confirmed our diagnosis of levosulpiride induced hyperprolactinemia. She was then prescribed with dexlansoprazole 60 mg once daily in empty stomach, mebeverine hydrochloride 200 mg twice daily, prucalopride 2mg once daily at bed time. She is doing well now and her galactorrhoea has completely subsided.

DISCUSSION

Drug induced galactorrhea is a condition of increased prolactin level in the serum caused due to adverse effect of a drug resulting in galactorrhea and irregular menstrual cycle in women. Levosulpiride is a novel drug with antipsychotic, anti-depressant, anti-emetic and anti-dyspeptic actions. Galactorrhea is the secretion of milky discharge from breast in men or women who are not breastfeeding for one year. It may result from excessive secretion of prolactin or increased sensitivity of breast tissue to prolactin.

Various causes of galactorrhea include medications like dopamine receptor antagonists (eg-phenothiazines, butyrophenones, risperidone, thioxanthenes, metoclopramide, sulpiride, pimozide), and dopamine depleting agents like methyldopa, reserpine etc. Other drugs like opiates, cimetidine, antihypertensives, isoniazide, danazol, verapamil, oestrogens and antiandrogens can also cause hyperprolactinemia. Herbal supplements such as fennel, anise and fenugreek seed are also supposed to cause galactorrhea.

History of a drug intake should always be elicited in all patients with galactorrhea or hyperprolactinemia before considering further evaluation. This would avoid the unnecessary costly investigations like MRI pituitary and unnecessary treatment with D2 agonists. However, a serum prolactin of >300 ng/ml is unlikely to be associated with prokinetic use and can be considered for the further evaluation of hyperprolactinemia.

Stopping the implicated drug for 72 hours or more and repeating serum prolactin level helps to confirm the drug-induced galactorrhea. However, it should be kept in mind that serum prolactin may not normalize by 72 hours in few patients and may take a week or more to do so.

Although D2 agonists can normalize prolactin in few patients with drug-induced hyperprolactinemia, it may often fail to reduce galactorrhea and/or hyperprolactinemia without stopping the implicated drug as observed in our study.[5] Hence, whenever feasible, stopping the galactorrhea-associated drug is the appropriate treatment for drug-induced galactorrhea and not the treatment with D2 agonists.

CONCLUSION

Levosulpiride is a potent inhibitor of D2 receptors in the anterior pituitary. Due to its increasing use as a prokinetic agent, more and more patients develop hyperprolactinemia as an unavoidable side effect. The magnitude of hyperprolactinemia is greater as compared to older antidopaminergic prokinetic agents. Awareness about levosulpiride and its effect on serum prolactin levels and careful drug history will help the clinician in reaching the exact diagnosis and avoiding unnecessary brain imaging.

CONFLICTS OF INTEREST

NONE.

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